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EXTRAPERITONEAL CESAREAN SECTION (GASTROELY-TROTOMY) IN PRESUMABLY INFECTED AND MISMAN-AGED CASES OF PROLONGED LABOR*

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THE methods by which a child can be delivered through the ab-dominal wall are still passing through a period of evolution and development. Many ingenious and different plans have been and still are being attempted. Some are found to be so lacking in merit that they soon, very properly, pass on into the discard. Some show many desirable advantages and yet are attended with serious dis-advantages. It is altogether probable that the best method of per-forming cesarean delivery has not, as yet, been attained. We hear much about the abuse of cesarean section to the exclusion of the other well-known methods of delivery. This criticism, certainly, does not apply justly to large well-conducted maternities. An abuse which we undoubtedly do witness, both in maternity hospital services and in cases under the care of private practitioners, is the failure to recognize early in given cases that delivery through the pelvis will be fraught with great danger to mother and child or else is impos-sible of accomplishment. If this were not true it would not have been possible for the writer to have seen, during the past March and April, within five weeks, eight cases in which craniotomy was the only thing left to be done. These eight well-developed, full-term fetuses were either already dead or so near dead that it would not have been possible to prepare an operating room quickly enough

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to give any promise of saving these children. The result was that eight, otherwise healthy, young women, except for the disproportion between pelvis and fetus, had passed through the risks and burdens of pregnancy, had been subjected to hours upon hours of ineffective labor and delivery by craniotomy. One mother lost her life; seven others, if so many survived, were childless. In seven of these cases the dystocia was due to either a well-marked funnel or male type pelvis. The eighth had a neoplasm, so situated that it made pelvic delivery impossible. These conditions should have been recognized during pregnancy, or at the latest early in the first stage of labor. Timely cesarean section was clearly indicated and would have saved these eight children and the mother who was lost. This is not a cry along a new trail. To go back not more than some seventy odd years, Cazeau, with rare comprehensive insight, pointed out the danger and objections to prolonged ineffective labor, especially with membranes ruptured. Nearly every textbook on obstetrics since his time reiterates the same thing, until we might properly write into obstetric history: "As it was in the beginning, is now"— Are we to continue so that the remainder of the quotation, "and ever shall be, world without end," is to be applicable?

Autopsies at the Lying-in Hospital upon stillborn infants and upon those who die soon after birth are revealing some instructive, if unpleasant, facts. It is found that the number of these children who die from cerebral hemorrhage, after unduly long labors which are eventually either terminated spontaneously or by forceps or version, is unwarrantably large. Similar cases, which have been under the care of private physicians have been admitted to the hospital after long labors, unknown attempts at operative delivery and examinations, but with a living child in fair to good condition. It is this type of case which gives the high maternal and fetal mortality following cesarean section. It is this type of case, with disproportion between fetus and pelvis, long labor, with ruptured membranes, unclean examination, unsuccessful attempts at operative delivery, which has made it impossible for me, in an experience of more than twenty-three years and somewhat over five hundred and eighty cesarean deliveries, to reduce my maternal mortality much below eight per cent, although at one time I could show nearly one hundred consecutive cesarean sections without a maternal death. The different members of the attending staff at the Lying-in Hospital, as seems best to each one, are attempting to cope with the presumably infected case, by a technic other than the classical cesarean section, which gives a very high mortality. Some favor the transperitoneal method, some the so-called double flap method; some a technic which is near or quite extraperitoneal.

I have employed the double flap technic in three cases and have lost one mother and her child. This mother gave one of the most

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In 1918 I began to employ, for these presumably septic, unfavorable cases, practically the technic of Thomas, which the latter called "gastroelytrotomy." I have used it in twenty-eight cases and have lost two mothers and seven children, three of which were stillborn and four died after delivery—a maternal mortality of 7.2 per cent, fetal mortality, 25 per cent.

Without any attempt at a review of the literature upon this subject, it may not be amiss to quote rather freely from what is found in the Fourth American Edition of Playfair's System of Midwifery, published in 1885, under the title, laparoelytrotomy. We learn that in 1820 Ritgen proposed laperoelytrotomy, leaving the peritoneum intact. He attempted such an operation unsuccessfully and was obliged to deliver his patient by caesarean section. In 1823 Beaudelocque the younger independently conceived and performed the same operation without success. In 1837 Sir Charles Bell conceived a similar operation, but there is no mention of his ever having performed it.

In 1870, Dr. T. Gaillard Thomas of New York read a paper before the Medical Association of the town of Yonkers, New York, entitled "Gastroelytrotomy, A Substitute For Cesarean Section," in which he described the operation which he had performed three times on dead subjects and once on a married woman with a successful issue as regards the child. It is further stated: "The object of the operation is to reach the cervix by incision through the lower part of the abdominal wall and upper part of the vagina, and through it extract the fetus as may most easily be done."

In a footnote we read as follows: "New York Medical Journal, Nov., 1878, Thomas operated twice, Skene four times, Charles Jewett of Brooklyn twice; Hime, Edis, Dandridge and Taylor of Cincinnati, and Walter R. Gillet of New York each once, in all 12; women saved, 6; children living but not moribund, 7; bladder lacerated in 6 cases. In properly calculating the risk of the operation it is fair to exclude the moribund case of Thomas, the intemperate and bedridden case of Hime and the diseased subject of Edis who survived, respectively, one hour, two hours and forty hours. The balance, nine cases, were favorable in four instances and unfavorable in five; six of the nine women recovered and five children were saved."

We may note in passing that while this operation is a much more difficult one to perform, the above results were far better than those obtained at that time by abdominal cesarean section.

THE THOMAS TECHNIC

"The abdominal incision extends from a point an inch above the anterior superior iliac spine, and is carried, with a slight downward curve, parallel to Poupart's ligament until it reaches a point one inch and three quarters above, and to the outside of, the spine of the pubes. Beyond this point it must not extend, in order to avoid wounding the round ligament and the epigastric artery. In this incision the skin, the aponeurosis of the external oblique, and the fibers of the internal oblique and the transversalis muscles are divided. The rectus is not implicated. After the transversalis fascia is divided the peritoneum is reached and readily lifted up intact, so as to expose the upper part of the vagina, through which the fetus is extracted." This report continues at considerable length in its description of the anatomic relations and development of the upper part of the vagina during late pregnancy and the difficulties and dangers attendant upon opening it—stating that in Beaudelocque's case, because he incised instead of tearing the vagina he was obliged to discontinue the operation on account of the loss of blood.

While the technic employed in operating upon the cases which I report is in principle, based on the foregoing as described by Dr. Thomas, it differs from it, I believe, in some essential particulars and results.

PRESENT TECHNIC

Starting at a point on a level with, and about 2 cm. to the left of, the right superior iliac spine an incision down to the aponeurosis of the external oblique muscle is extended obliquely downward and inward to the middle line parallel to, and slightly above, Poupart's ligament, the inner end being slightly above the spine of the pubes. As the superficial epigastric artery and other vessels come into view they are double clamped, divided and ligated. It has been found that this is a time saving precaution, in that it keeps the field of operation clear. The edges of the wound are retracted and in succession the remaining layers of the abdominal wall are divided, where possible separating the fibers. The transversalis fascia is opened the whole length of the wound. Passing the hand close to the posterior surface of the front wall of the bony pelvis the bulging peritoneum can be readily lifted, and, covered with a pad moistened in warm salt solution, is held out of the way in the upper and outer part of the wound by a retractor. No attempt is made to expose or open the vagina, although it is sometimes opened for a short distance in cases where more room is needed. The bladder is more readily manipulated if it contains just enough fluid to give it outline. With a boring movement of the fingers at the upper and right margin of the exposed portion of the bladder, its posterior wall is readily reached and an easy line of cleavage is found. Passing the fingers up to the uterovesical fold the bladder can readily be freed from above downward and to the left. This exposes the anterior portion of the lower uterine segment, a large area in a pregnant uterus developed to full term. While a wound of the size and location as described is necessary, it is well, in so far as possible, to keep manipulations away from the outer end of the opening. In my hands, failure to do this has several times resulted in such complications as making a small opening through the peritoneum, tearing across the circumflex iliac artery, resulting in annoying delay from a wound quickly filled with blood, and the necessity to find and ligate the bleeding point, and the undue exposure to injury of the external iliac artery.

Considerably more room can be gained by partially dividing the tendon of the right rectus and the pyramidalis muscles rather close to the right pubic

spine. The bladder is covered with a moist pad and retracted downward and to the left. The exposed portion of the uterus is thinned and bulged forward by the presenting part of the fetus. Retracting the wound as far as possible to the left a vertical incision is made close to the left side of the abdominal opening and from below the uterovesical fold downward far enough to furnish an opening sufficiently large to allow the delivery of the fetus. Sometimes, but not in all cases, this opening extends into the upper part of the vagina. At this time it is well to take a culture from beside the presenting part of the child. By this location of the uterine opening as described, and by the usual dextrotorsion of the uterus, should this opening be extended by laceration during the delivery of the fetus, there is less likelihood that the uterine artery will be reached and torn across. In my earlier operations this accident happened in several cases. Proceeding now with the delivery;—forceps were usually applied, but except in two or three instances delivery has proved unsuccessful by this means. Nearly all of the children have been delivered by internal podalic version and breech extraction, followed immediately by manual extraction of the placenta and membranes. Unless more than usual precautions are observed, the overstrained but now relaxed uterus is more than likely to give an exhibition of several quick profuse hemorrhages in which the total loss of blood is considerable. The fundus should be promptly held and 1 c.c. of pituitary extract should be injected deep into the muscles of the thigh. From observation and experience I have reached the confirmed belief that pituitary extract should have no place in obstetric practice until the uterus is empty. In case a portion of the vagina is opened and annoying bleeding results from the cut edges, this can be overcome by digital compression or by several deep temporary sutures passed parallel to, but well back from, the edges of the wound, to be removed after permanent closure.

The opening in the uterus is closed by two or three layers of sutures with a continuous suture close to the deep edges of the uterine wall. Several interrupted sutures and a continuous Lembert suture complete this part of the operation. Sometimes the uterus has so thinned that it is difficult to find room for three layers. The bladder and peritoneum are allowed to resume their normal location.

The divided portion of the tendon of the right rectus and the pyramidalis muscle are carefully approximated and secured by several interrupted chromic sutures. A continuous suture closes the transversalis fascia; another layer of interrupted sutures secures the muscle fibers. The edges of the aponeurosis of the external oblique muscle are overlapped by the use of the mattress sutures and the free edge secured by a continuous suture. The remainder of the wound is closed with silkworm gut sutures. In earlier cases I employed strands of chromic gut or rubber tissue carried down to the fascia. Soon I abandoned the use of any drains. No better results were obtained with than without drainage.

It should be borne in mind that all of the cases herewith reported were septic to a greater or less degree. All of these cases had high temperatures after operation. In no case was it possible to secure primary union of the abdominal wound. Two showed only an oily discharge for a day or two from two or three stitch holes. In twenty-one cases, part, or the whole length of the wound separated down to the aponeurosis. In four cases the whole depth of the wound broke down with considerable sloughing. Two patients died early before the repair process had time to exhibit what would have hap-

pened. The wounds healed readily, and in all cases the infection remained local, with the exception of two or three cases in which there was mild tenderness down the inner part of the right thigh, as of a very slight phlebitis. I have had no evidence that the uterus was infected, or that its wound failed to unite by primary union. In a few of the cases there must have been a very localized peritonitis. With the exception of one case, either by symptoms or leakage, there has never been any suggestion that the bladder had been injured or later became infected. One case which sloughed badly had a vesical fistula for a short time, which soon closed spontaneously.

It is not surprising that considerable fat necrosis occurred in many of the cases from traumatism due to retraction. Because of open wounds the stay in the hospital was usually quite prolonged. In four cases, we freshened the granulating surfaces and the skin edges, and resutured the wound after sloughing had ceased. Healing was almost perfect in every case and the necessary stay in the hospital was considerably shortened. All of these patients were tired out and exhausted.

The operation is physically and technically a very difficult one to perform. In early cases, I spent something over two hours, later being able to perform this operation in about fifty-five minutes. Much time was lost because of the failure to secure bleeding points before or at once after vessels were cut. Very much more time was lost before I learned how to detach the peritoneum and also in the attempt to detach and separate the bladder along its right side, where the line of cleavage is not distinct. Notwithstanding the previous condition of these patients, and the fact that they were subjected to a long difficult operation, their early postoperative condition was remarkably good. Vomiting was never a distressing symptom, and abdominal distension was almost entirely absent.

In Dr. Thomas' report, considerable stress is laid upon the danger of injuring the deep epigastric artery. From early reports, opening into the bladder was rather a common accident. I cannot recall that the deep epigastric artery ever came into view or was injured in any of the cases. In one case only there appeared a urinary fistula. This became evident after the tenth day postoperative, and was believed to have been due to the neighboring sloughing. In two cases the right round ligament, and in one, the right ureter, were innocently in evidence. They caused no inconvenience, and so far as I was able to determine they suffered no injury. Usually the widely expanded pregnant uterus tends to carry these structures far out to the sides and out of the way.

Some of the more salient points of interest in connection with these cases are that there were sixteen primiparae, one para ii, five para

iii, one para iv, one para v, one para vi, two para vii, and one para viii. The ages ranged from seventeen to forty-one. Twelve of these cases were wholly under the care of the Lying-in Hospital. The remaining sixteen had been under the care of other physicians and midwives for an unknown number of hours. Of the two mothers who died, one was forty-one years of age, and a para viii. She had been under the care of an outside physician, and a midwife. She gave a history of having had three living children. The first was stillborn; an instrumental delivery. The others were difficult deliveries. The second was a small sized child, the third was a large child, the fourth of medium size and difficult delivery. She had also had three abortions in the third month of pregnancy. In the labor under consideration the child weighed 4,160 grams and lived. The mother died on the second day, of general peritonitis. There was serosanguineous fluid in the peritoneal cavity and cultures showed hemolytic streptococci. This woman had a contracted pelvis, and reported that all of the living children had been injured by the stretching of the brachial plexus.

The other patient who died was twenty-seven years old, a para i, who had had outside medical attendance for an unknown number of hours before admission. A forceps delivery had been attempted. The patient gave a history of having had pneumonia three weeks before labor. Her child weighed 2,020 grams and lived. She was in poor condition on admission, and it was my impression that the cause of her death was pneumonia plus labor, rather than the reverse. No culture was taken in this case.

In all of the twenty-eight cases reported the fetal heart was heard just before operation was begun. Three babies were stillborn. In these cases there was marked tonic contraction of the uterus, and evidence of fetal distress as indicated by the escape of meconium and a varying fetal heart. In one of these stillbirths, the mother was a girl of seventeen years, who had been under the care of an outside physician, and a midwife. Hydrocephalus and spina bifida were found in the child. It was a face presentation.

Four babies died. One child died after four and a half days; another on the nineteenth day from a very extensive pemphigus. The mother in this case showed a four plus Wassermann reaction. The third child weighed 4,870 grams and died on the labor day; the autopsy showed atelectasis and asphyxia. The patient had been in labor for a long while prior to admission to hospital. The fetal heart was from 140 to 180 prior to operation. In the case of the fourth child, labor was said to have been in progress for three and a half days under outside care. The child weighed 3,400 grams, and died six hours after delivery.

All of the cases wholly under the care of the Lying-in Hospital, with trial labor going on for so long a time, and in some instances attempted forceps delivery, had been for this reason rendered unsuitable cases for classical cesarean section. All of these mothers survived. A stillbirth occurred in one case after sixteen hours' labor. One child died on the nineteenth day from pemphigus; the mother was syphilitic.

Six of these patients in a subsequent pregnancy have come under my care. One in the third month, when assured that she was pregnant, declared that her husband demanded that she should have abortion induced. Nothing further has been learned about her. The other five continued to the full term of pregnancy. One had an almost precipitate spontaneous delivery of a very small child. Four others were delivered by me, by classical cesarean section. Bimanually, with one hand through the cesarean opening in the uterus, the site of the former extraperitoneal operation was carefully examined in each case. It was rather surprising to find how well the uterine wall had closed and how little in evidence were adhesions in the neighborhood. In no instance was there found any weakening or hernia at the site of the former opening in the abdominal wall.

I am more and more impressed with the importance of securing the essential points in the history of every pregnant woman. The primiparous patient is an unknown quantity, obstetrically speaking, but in her case it is important to learn whether she has any history of disease, previous illness, or operations, which may have some bearing upon the course of her pregnancy and approaching confinement. This likewise holds true of the multiparous women, but also a searching inquiry should be made into her previous obstetric history. In women who are able to develop a fetus through pregnancy and into labor, with our present knowledge and equipment it should be impossible to find histories of two, three, four, and in one of our cases, of five consecutive stillbirths or the delivery of injured children who soon die, and certain others who are not so fortunate as to die, but are elected, because of birth injuries, to materially swell the ranks of the incompetent and to overcrowd institutions for the crippled and feeble minded. Patients giving histories of difficult or operative deliveries with bad results should be examined as to the cause of this. They should be watched with unusual care in each individual case. Some means should be found by which the previous course should not be repeated, even delivery by cesarean section if that is the best procedure in a given case. But the condition should be foreseen and provided for.

After the patient's history has been taken there should be a general examination sufficiently thorough to indicate whether she is suffering

from pulmonary or cardiac disease. Then should follow the routine obstetric examinations, which should include height, weight, breasts and nipples, abdominal measurements, palpation, and auscultation for the fetal heart, external and internal pelvimetry, blood pressure, urinalysis and the Wassermann test. I find that about 2 per cent of all applicants at the Lying-In Hospital, show a positive Wassermann reaction.

Pelvimetry is important and should in no sense be neglected. Patients having contracted pelves, should be under careful observation. If they are given the opportunity and the observation be close enough, we shall see that a large proportion of such cases will deliver themselves without assistance, or at most, by the aid of easy forceps. The remainder of such cases have either declared themselves by their former history, or they soon make it evident that they require some form of operative assistance—forceps, version or cesarean section. Many of the patients with distorted and contracted pelves habitually give birth to small children; often the skull bones are thin and capable of being dented like a sheet of celluloid; they have wide suture spaces; the fontanelles are large. Such heads will mold and pass through surprisingly contracted pelves. In former times we were instructed: Given such and such pelvic measurements, such and such management of a case should be carried out.

We still see, from time to time, publications giving this same sort of advice. The wise obstetrician will do nothing of the sort. He will take pelvic measurements as he would a laboratory report as a part of the data in the individual case under observation at the time, and from the previous history, from the measurements, from the contour, muscular make-up of the uterus and abdomen and their driving force, and above all from the size, shape and moldability of the fetal head, he will decide whether that particular head will pass through that particular pelvis. If his stock of wisdom still holds out and he considers the interest of mother and child and his own peace of mind, he will determine this fairly early, before the patient is exhausted and the fetus shows signs of distress, and the liability to infection has been increased by ruptured membranes and manipulations. It is becoming fairly easy to detect these cases with contracted pelves, or disproportion between pelvis and vertex, which will require some form of operative assistance in delivery. It has seemed to me that this type is rather decreasing in numbers.

There is another distinct type, seen much more frequently than formerly, and far too little called to notice by teachers and writers. I refer to the woman having the male type or funnel pelvis. They are difficult to detect and they require the keenest kind of obstetric judgment and skill to carry a given case of this kind through labor with safety and success for mother and child. Here pelvimetry gives no assistance whatever. These patients are usually of medium height, stocky build, with apparently broad hips. They have

the appearance of robust health and vigor.   They are well nourished, buttocks and hips especially are made up chiefly of large cushions of fat.   Their external pelvic measurements are up to or above normal. The lumbosacral angle is accentuated.   A horizontal plane passing through the promontory and another through the symphysis pubes are far apart.   The pelvic bones are thick and strong.   The pubic arch may or may not be narrowed.   The internal, diagonal conjugate, if the promontory can be reached, not infrequently measures twelve or more centimeters.   Sometimes the contour of the pelvis below the inlet is well formed and of ample capacity.   In other cases one or both of the side walls of the true pelvis are flat and tend to converge.   The pelvic inlet would be ample for an ordinary moldable vertex, and in many of the cases, if a large part of the vertex would pass through the inlet with a fully dilated cervix, there would be comparatively little difficulty in completing pelvic delivery.   But the pelvic make-up and capacity is but one side of the equation.   Such patients habitually give birth to large children with hard, square block-like heads, with thick dense cranial bones and suture lines and fontanelles which are hardly discernable.   Membranes are apt to rupture before or soon after the onset of labor.   Posterior positions are rather frequent.   Such cases are deceptive because a considerable segment of the vertex sets into the inlet like a ball valve; it does not advance.   Such dilatation and thinning of the cervix as takes place is slow.   In many cases labor is neither continuous nor vigorous.   One is apt to be misled by the hope that active progressive labor will soon begin resulting in dilatation of the cervix and advance on the head.   Such cases are apt to develop tonic contraction of the uterus and thin out the lower uterine segment, risking rupture of the uterus, compressing the vertex down against the inlet and the placenta against the child.   As if this were not danger enough, far too many of these cases are given pituitrin at this stage.   It would be bad practice to give ergot under such conditions, but pituitrin, which acts with great suddenness and force within four minutes after its injection, as I have repeatedly witnessed in cesarean operations, after the uterus was empty, by some strange reasoning, in the minds of not a few, appears to be good treatment.   These cases are difficult and dangerous for mother and child; they belong in a hospital.   They certainly should not be attempted single-handed and alone in the patient's home. In many of them if pelvic delivery, dilatation and incisions of cervix and forceps are persisted in, the operator does not usually look upon his completed work with pride.   If version is attempted, too often the results are not good.   Many of them become unsafe, because of the risk of sepsis, for classical cesarean section, unless this is done early.   This type of case gives the high percentage of stillbirths, cerebral hemorrhage, broken necks, children in whom the heart continues to beat for an hour more or less, and yet it is impossible to start respiration, or

those who die soon after birth. Would it not be better to foresee some of this early and "abuse" cesarean section in more of these cases and do it early when it is comparatively safe for mother and child? If the mothers are made to understand, there is no doubt regarding the answer which they will give.

RÉSUMÉ AND CONCLUSIONS

1. The sooner the general public, both lay and medical, come to the realization that reproduction is potentially, and in ten per cent of the cases, actually a pathologic process, and act accordingly, the sooner childbed will be removed from the position which it now holds in this country as, next to tuberculosis, the cause of the greatest number of deaths.

2. Every pregnant woman should be under competent obstetric care and instruction soon after conception, through gestation, labor and the puerperium, which should continue until everything possible has been done to restore her to her normal activities of life in good condition. Ninety per cent of pregnant women should be under careful observation, but aside from a few simple precautions and instructions, as long as they are progressing favorably, should be treated to a very generous share of masterful letting alone. It should always be kept in mind that some from this larger class have a way of moving, gradually or abruptly over into the abnormal class.

3. The emergency obstetric case should disappear. It is this type of case which magnifies the morbidity and mortality of obstetric records. So long as such cases do occur, the well equipped maternity hospital should receive them, even though they are apparently about to die. With such aid, some of the seemingly hopeless cases will recover. There should be some way of checking up the activities of the doctor who is repeatedly showing bad results. Such an one should be rather actively encouraged to direct his energies along less dangerous lines.

4. We can often see more by looking backward. We would accomplish more, with better results, by looking ahead. Preventive obstetrics should be a widely broadcasted slogan. The public should be taught to be more critical of obstetric result, and not to so complacently accept dreadful injuries to mother and child, or death of one or both, as the Will of an overworked Providence. Extraperitoneal cesarean section will save some lives that would otherwise be lost. Classical cesarean would have saved but few of the cases reported.

44 PARK AVENUE.

IS CESAREAN SECTION JUSTIFIABLE IN ABLATIO PLACENTAE?*

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PREMATURE separation or ablatio placentae (Holmes) is the partial or complete separation of the placenta from the upper segment of the uterus during pregnancy or during labor, before completion of the second stage, due to some pathologic state of the uteroplacental union, or to violence done to the organ.

In my experience, premature separation of the normally implanted placenta is perhaps the most frequent cause of antepartum bleeding at or near term; and it is an accident which all of us should be prepared to recognize and treat along rational lines; for but few cases require radical interference, but all need intelligent supervision.

The frequency of ablatio has been estimated as about 1 in 200 labors; however, I am under the impression that many cases of partial separation with concealed hemorrhage are missed, owing to careless observation, and that many of the cases that are diagnosed as partial placenta previa, because of the occurrence of bleeding, near term or during labor, are really premature separation.

In our clinic where every placenta is carefully examined, we have been surprised to find how many placentae have old blood clots on the maternal surface; hence we have come to feel that ablatio is seen more frequently than placenta previa. The factors which seem to predispose to this accident are age, multiparity, advanced period of pregnancy, and the unstable attachment of the placenta due to the physiologic structure of the serotina at, or near term.

Upon reviewing my cases I found that the majority of these accidents have occurred in women between 25 and 35 years of age, who have had an *antepartum history of toxemia;* while the minority have shown evidences of deciduitis or placentitis with hemorrhages in the serotina, and but a few could be attributed to direct violence, as blows, kicks or sudden muscular exertion.

The point and degree of separation have considerable bearing on the amount of blood which the patient loses and the severity of her symptoms; consequently they must also have some bearing on the prognosis and form of treatment which should be instituted.

As I have already stated, the normally situated placenta may become

(1) partially or (2) completely separated from its placental site. If the
former, the separation may be central (Fig. 1), the placenta remaining
attached at its circumference, which allows the formations of a retro-
placental blood accumulation.   This stimulates contractions which in
turn compress the clot and further separate the placenta from its at-
tachment, so that one edge may separate and the escaping blood strip
the membranes from their uterine adhesion.
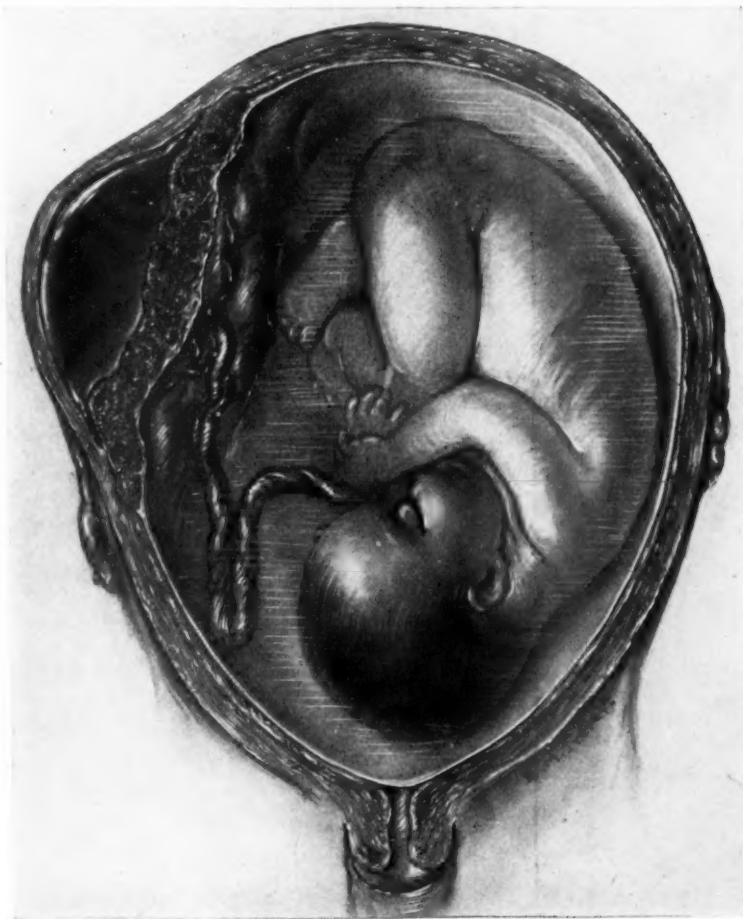
Fig. 1.—Central separation.   Concealed hemorrhage.

It may be stated that *all cases begin with absolute concealment of
the hemorrhage* and later, may develop an apparent hemorrhage; for
as the membranes are detached from the lower uterine segment, there
may be an apparent hemorrhage when the presenting part does not
completely block the lower segment (Fig. 2), blood and clots escaping
at the time of contractions, or the blood may remain concealed if the
presenting-part is engaged, and completely blocks the cervix.   In this

case blood can be demonstrated by the escape of serum, blood, or clots, when the presenting-part is displaced upward on vaginal examination (Fig. 3). When the separation is complete, the accumulation may rapidly distend the uterus; for the placental site in an overdistended spastic uterus cannot retract unless the membranes are

Fig. 2.—Apparent hemorrhage, **partial separation**. Head unengaged.

ruptured soon after the separation takes place, for the increased intrauterine bulk prevents thickening of the uterine walls by normal retraction.

While pathologically there seem to be two types—the one (Fig. 4) with concealed, and the other with apparent bleeding—this difference is only relative, or one of degree.

The diagnosis should be readily made upon the symptom complex, which is almost always present.   The patient, an old primipara, or a multipara, usually at, or near term, who may have shown some of the prodromal signs of toxemia (such as a trace of albumin in the urine, or a rise in the systolic blood pressure, or these signs may have been absent)

Fig. 3.—Head filling lower uterine segment, preventing escape of blood.

is suddenly seized with cramp-like uterine pain, which may be localized and referred to the placental site, faintness, or nausea, which is always attended with some degree of shock, blanching, and pulse rise.   Palpation shows a uterus that is extremely sensitive, spastic, tense and firm, or flaccidly filled with retained blood which does not intermittently contract and relax, as in normal labor.   The fetal movements may be tumultuous and then cease, depending on the degree of separation.

Owing to the spasticity of the uterus, detection of the fetal parts is difficult. Auscultation will show the fetal heart to be absent if the ablatio is complete, or if the separation is incomplete there will be progressive signs of impairment in the fetoplacental circulation—of course

Fig. 4.—Complete separation—distended, atonic uterine wall becoming thinner.

both the fetal movements and the changes in the heart sounds are dependent on the amount of separation.

The diagnosis is confirmed in both the relatively concealed, and in the apparent cases by the escape of bloody serum, or by actual vaginal

hemorrhage. In the relatively concealed cases, on raising the present-ing-part out of the pelvis, it is usual for some of the accumulated blood and clots to escape into the vagina, while palpation and mensuration will demonstrate the asymmetry, or the rapid enlargement of the uterus (Fig. 5).

It is my purpose, in this short communication to outline the obstetric procedures indicated in the management of this accident, for like ectopic, the cases may be divided into those in the nontragic, and those in the tragic stages.
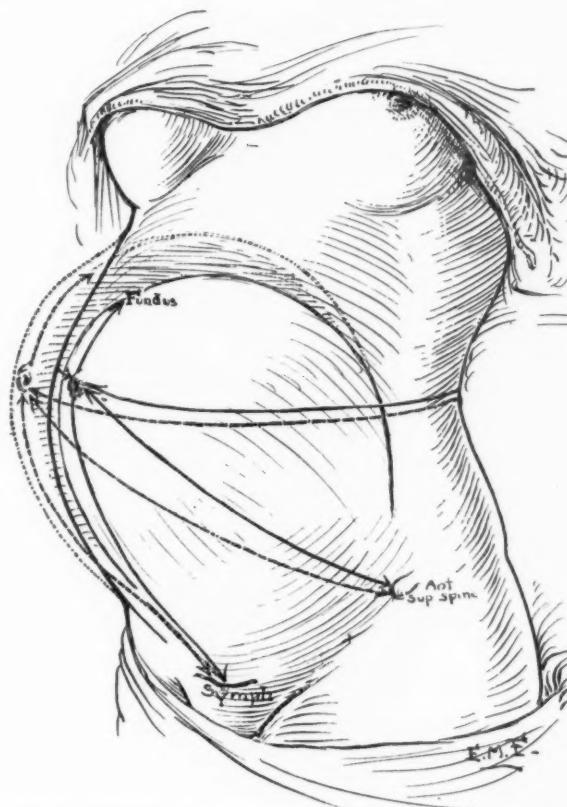
Fig. 5.—Mensuration showing the rapid increase in size of uterus with retained blood.

Clinical study of a large number of these cases has shown that it is possible to differentiate between those that can be safely treated on the expectant plan, and those that require rapid infrapelvic delivery, or sec-tion and hysterectomy. The treatment depends largely on the extent of the pathology, and while today, in many instances of separation, there seems to be irrefutable evidence of an associated toxemia, there are others which cannot be attributed to this cause.

Morse's observations confirmed by his experimental work on rabbits, in which he tied all three groups of the efferent veins of the uterus on

one side, seem to prove that the exciting cause of many of these separa-
tions may be attributed to placental apoplexy produced by sudden
uterine torsion which interferes with the out-going blood. One has but
to remember the picture of the uterine veins of the pregnant uterus when
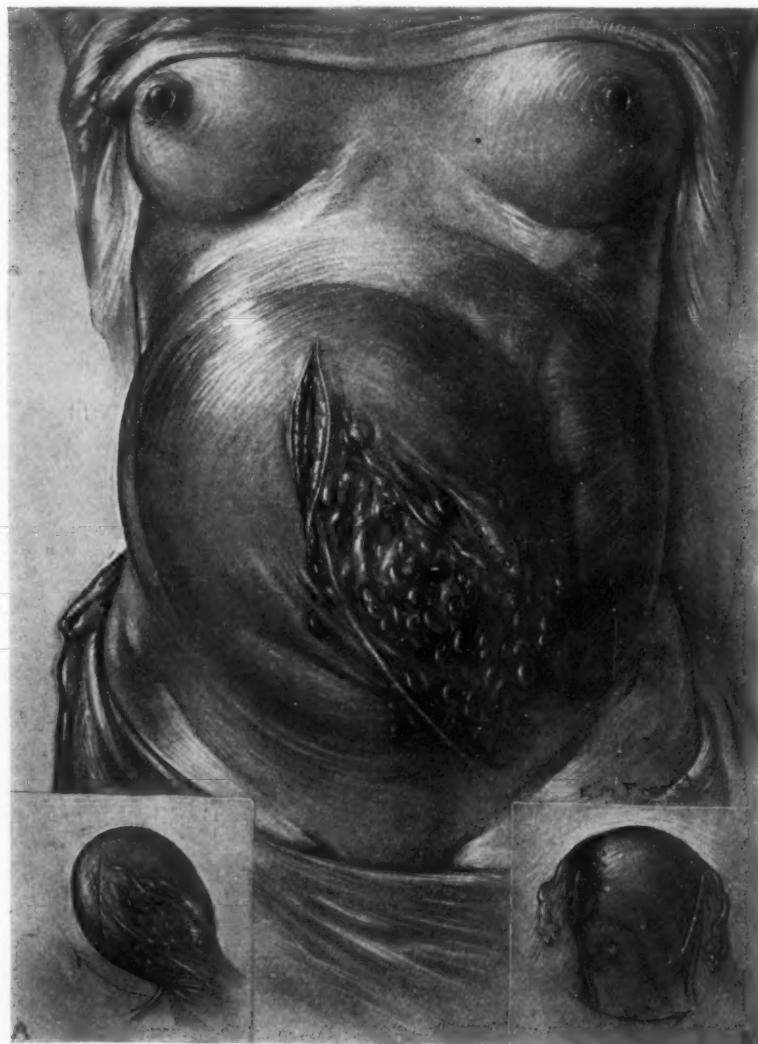
Fig. 6.—Extreme torsion of uterus.

the abdomen is opened at section, to realize how increased torsion of the
uterus, near term, may block the venous return on one side (Fig. 6), and
engorge the mesometric veins, the intervillus spaces and the decidual
radicals. This torsion when it is greater than normal may be further
increased by muscular effort or by uterine contractions of the torsioned
uterus. This naturally further engorges the large veins on one side,

and engorges the vessels in the serotina which act exactly as does retraction of the uterus during the third stage of labor, namely, allows hemorrhagic extravasations to take place at many points in the spongy layer of the decidua which during contraction further separate placental attachment in the so-called concealed type. Owing to the fact that the placental site cannot retract because of the bulk of the uterine content, the area behind the placenta becomes distended with blood, fluctuant then spastic and very tender. If the placenta completely separates, retraction of the site may not take place as long as the uterine content prevents diminution in the size of the uterus. Consequently, instead of the uterine wall thickening, the walls become thinner and more atonic as the bleeding from the placental site continues and the blood accumulates in the space between the membranes and the uterine walls, always increasing the size of the uterus; hence, continued intrauterine bleeding may be demonstrated clinically by repeated mensuration of the uterus, record of the rising pulse rate, persistent fall in the systolic blood pressure, and progressive drop in the hemoglobin percentage. While objectively the patient continues to show more pallor and other external evidences of internal hemorrhage, such a picture does not brook expectancy, but needs prompt surgical intervention with coincident blood transfusion.

On the other hand, the nontragic cases likewise present a typical syndrome which may be readily recognized i. e., a pregnant woman at, or near term, who after exertion, or without appreciable muscular effort, except perhaps a few uterine contractions, is seized with cramp-like uterine pain, slight collapse evidenced by nausea, pallor with perspiration about the lips, nose and forehead, lowering of the blood pressure, and increased pulse rate. On physical examination the uterus will be found to be tense and tender, and may be asymmetrical if the blood has accumulated behind the placenta (accessory tumor) or with the occurrence of pain, vaginal bleeding may be apparent, or only be demonstrated on making a vaginal examination and raising the presenting-part which liberates some accumulated blood clots.

Given a patient presenting the foregoing picture, and excluding placenta previa by the absence of its physical signs, a diagnosis of ablatio placentae may be readily made. Such a patient should be immediately transferred to the hospital and allowed a short period of intelligent observation. If the cervix is effaced, or the patient is a multipara, the membranes may be ruptured and the bulk of the uterine contents diminished. This theoretically allows the fetus to act as an intrauterine tampon which stimulates muscular contraction. A quarter to a half a grain of morphine is administered to relieve the shock and aid in the dilatation, while a tight many tailed abdominal binder is applied from above downward in order to firmly compress the uterine wall against the fetal tampon. In addition to this, the vagina may be firmly

piugged with sterile gauze or cotton moistened with boroglycerid which further stimulates uterine contractions and favors dilatation.

If it is certain that the pelvic measurements at the outlet are ample, the presenting-part is engaged, and there is already evident dilatation of the cervix, the suggestion of Tweedy, of giving small repeated doses of pituitary extract every 20 minutes, will further aid the control of bleeding.

During this watching period intelligent observation is imperative. The pulse should be taken and recorded every fifteen minutes, the systolic pressure every half hour, and the hemoglobin and red cell count every hour, while the height and size of the uterus which has been carefully marked out upon the abdomen, should be noted and any increase in uterine distension recorded. If these measures check the hemorrhage, as they usually do in the majority of cases, the pulse will gradually improve in quality and become slower, the systolic pressure will rise or remain stationary, and there will be no further fall in the hemoglobin percentage until delivery occurs and the placenta is expelled. If, however, the pulse rate is high, I have found it wise to firmly pack the interior of the uterus with washed iodoform gauze and thus control further oozing.

On the other hand, if the intrauterine bleeding is continuing, the uterus will further enlarge, or the outward flow of blood will not be checked. It must be remembered however, that the amount of vaginal bleeding is no index of the amount of blood lost; for more or less blood is always retained within the uterus. The pulse increases in rapidity and diminishes in quality, while the systolic pressure will slowly fall as will also the percentage of hemoglobin.

In those patients, in whom the clinical picture above described, show the signs of progressive intrauterine bleeding, no infravaginal method of delivery is justifiable unless the cervix is already dilated. For one is dealing not only with the atonic uterus, but with an organ whose musculature presents definite pathology, namely, an apoplectic uterus with blood extravasations into the myometrium causing disassociation of the muscle fibers making it impossible to secure retraction, and hence postpartum hemorrhage is the sequel (Fig. 8). Furthermore, the release of the large quantity of retained blood which immediately follows delivery of the fetus, is always attended with severe shock, for the rapid emptying of the overdistended atonic uterine cavity does not permit of retraction, hence, the frequency of fatal collapse. I formerly delivered these patients by manual cervical dilatation, forceps and version, and saw them collapse after the fetus was expelled, with a postpartum gush so torrential as to be uncontrollable.

As in ectopic, the woman may sensitize herself to a certain amount of blood loss, and if further bleeding is permanently controlled, even 'f she is pulseless, she will show signs of reaction. But, if in addition

to this great blood loss, any further bleeding continues, she will fail to react, for shock and hemorrhage are interdependent, and these patients are already severely shocked. Hence, I feel that surgical trauma which is attended by any further blood loss must result fatally.

What then should be the attitude in the management of these tragic cases, what will determine the plan of procedure? This will depend largely on the condition of the patient, and the condition of the cervix, for the child is a negligible factor. One is not justified in doing a cesarean section which will entail further shock and oozing to deliver

Fig. 7.—Torsion shown by position of uterine incision. Ecchymotic areas in wall.

a stillborn child, unless one is prepared first to transfuse the patient, and then prevent further blood loss by hysterectomy. Section upon this type of case has always revealed a constant pathologic picture—large areas of the uterine wall are ecchymotic (Fig. 7) and when cut through do not bleed, but ooze serum and microscopically show multiple thrombosis of the vessels of the myometrium, distorting and disintegrating the muscle fibers. (Figs. 8, 9.)

There is extreme flaccidity with little or no tendency to uterine contraction and retraction; hence, retention of the uterus necessarily

means continuation of the oozing and frequently infection, for it is exceptional that these patients have not been repeatedly examined through the vagina before admission to the hospital.

It has been my practice to prepare the patient during the observa-

Fig. 8.—Section showing hemorrhage into muscle wall and thrombosis.

Fig. 9.—Showing large thrombus in a torsioned uterus.

tion period for possible immediate operation, and secure a donor for blood transfusion by one of the direct methods, such as suggested by Unger or Miller. Experience has taught us that it is good surgical judgment to transfuse these patients before active surgery is

done upon them, or to have the transfusion coincident with such surgery. Of course, if the cervix is well dilated, the presenting-part engaged and the woman is actually in labor, a few minims of pituitary extract with a tight abdominal binder will expedite the labor; but this is not the class of case under consideration.

In the majority of these tragic cases, the unprepared cervix offers an obstacle to infrapelvic delivery; hence, it has been my plan after first transfusing the patient, to open the abdomen with a long median incision and eventrate the uterus. Inspection will immediately show whether it requires removal or can be safely left *in situ;* for the apoplectic uterus shows numerous ecchymotic areas and fails to contract. In the presence of such a condition, the child is invariably dead, therefore, it has been my practice to clamp both broad ligaments in order to control the uterine and ovarian blood supply before incising the uterus; this permits the performance of a bloodless supracervical hysterectomy. On the other hand, if there are fetal heartsounds, and inspection of the uterus shows no intermuscular hemorrhages which are evidenced by ecchymotic areas under the perimetrium, and the uterus intermittently contracts, hysterotomy, leaving an intrauterine pack within the cavity, is a justifiable procedure.

From this study it is fair to assume:

First, that ablatio is a relatively common accident.

Second, that previous toxemia is a predisposing factor.

Third, that many of the cases have an apoplectic origin from torsion of the uterus, while very few can be attributed to trauma.

Fourth, that the symptom complex is constantly present and makes the diagnosis, which may be confirmed on vaginal examination by the escape of serum, blood or clots.

Fifth, that clinically this accident presents two general classes, the nontragic and the tragic cases.

Sixth, that in the former, intelligent expectancy in conjunction with rupture of the membranes, a tight abdominal binder, and pituitary extract will effect spontaneous delivery.

Seventh, that in the tragic cases which show progressive hemorrhage, fall in blood pressure and hemoglobin percentage, section after transfusion is the procedure of choice.

Finally, the decision between hysterotomy or hysterectomy depends on the condition of the uterine muscle.

20 LIVINGSTON STREET.

I. FROZEN SECTIONS THROUGH UTERUS OF WOMAN DYING DURING THIRD STAGE OF LABOR, ILLUSTRATING MECHANISM OF PLACENTAL SEPARATION AND EXTRUSION. II. FROZEN SECTIONS THROUGH UTERUS OF WOMAN DYING FROM CENTRAL PLACENTA PREVIA, FOLLOWING BRAXTON-HICKS VERSION*

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THESE specimens are of considerable pathologic interest, but since they have been so clearly reproduced in the accompanying illustrations by Mr. W. B. McNett of Johns Hopkins it is necessary to do little more than briefly outline the history of each case, and point out in an explanatory way certain particularly important features of each specimen.

CASE 1.—Mrs. D. W. H. (Hosp. No. 6167-1916) was a primipara, nineteen years of age. Upon admission to the hospital she was moribund with advanced edema of the lungs, dyspnea, a pulse rate inaccurately determined at about 160, and in fact, every symptom of acute cardiac decompensation. The head of a six and a half months' fetus was showing at the vulva, and had been visible for one hour previous to admission, according to the report of Dr. J. N. Stanton who had been called to see the patient for the first time a few hours earlier.

The symptoms developed acutely at 3 A. M., this being about the time her labor began. She entered the hospital at 6:45 A. M., and without anesthesia the head was lifted out with forceps a few minutes later, the patient dying two minutes after the birth of the fetus (7:30 A. M.).

The autopsy showed edema throughout both lungs, acute exacerbation of chronic nephritis, and acute dilatation of the heart. The uterus with the placenta *in situ,* the bladder, part of the vagina and rectum were removed, frozen and longitudinal sections cut.

The sections illustrate normal placental separation and extrusion according to the mechanism of Schultze, but it is noteworthy that there is no evidence of the retroplacental hematoma which is so generally considered essential to the extrusion of the placenta by this mechanism. (Figs. 1 and 2.)

According to Williams' "Obstetrics," Baudelocque in 1789 described the two ways in which the placenta may be extruded, saying, "In the first case the middle of the placenta being pushed forward by an

effusion of blood beneath it, the organ becomes inverted upon itself in such a manner that it presents by its fetal surface, et cetera.'' Schultze's name was attached to this mechanism in 1865, when he advanced the opinion that the placenta was usually expelled by the
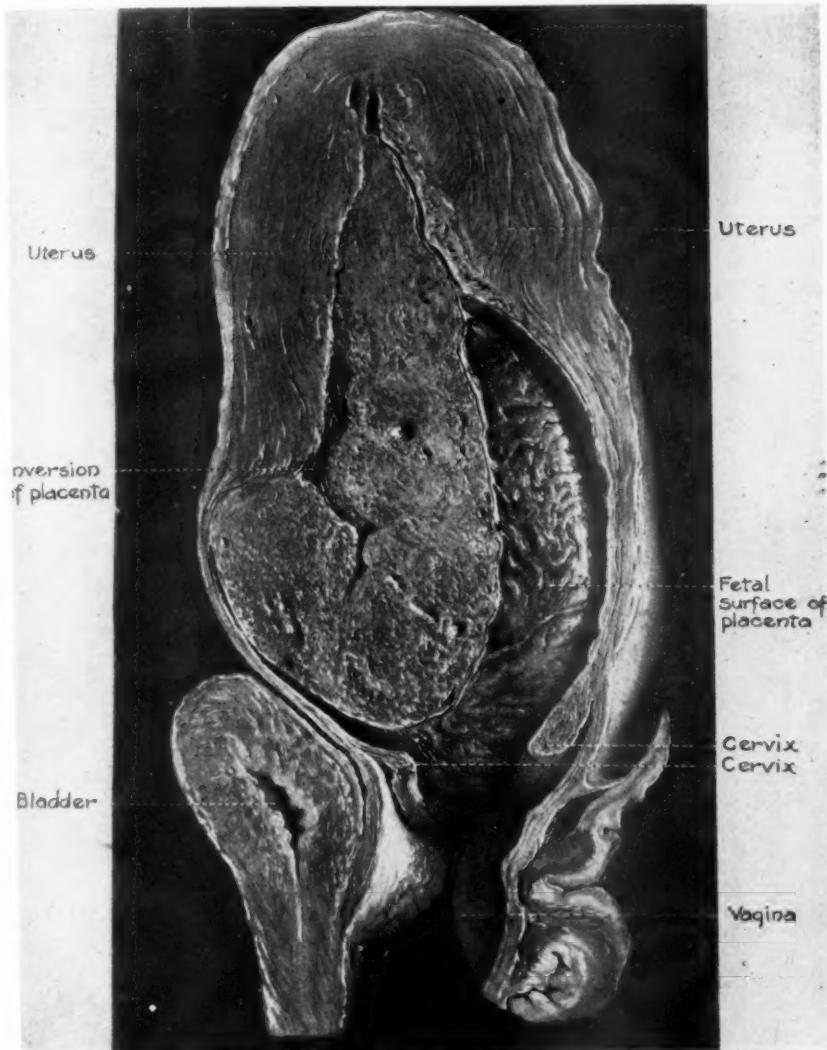
Fig. 1.—Third stage of labor. Right half of uterus. Placenta partly separated, and inverted, with fetal surface presenting at os. Unequal contraction of fundus indicates placental separation by muscular contraction with absence of the traditional retroplacental hematoma.

first method described by Baudelocque. Williams and others subscribed to these views, crediting the formation of a retroplacental hematoma of considerable size with practically all of the separation of the placenta from its site.

Fig. 1 shows the right half of the uterus with the placenta suffi-
ciently separated and inverted that by uterine contraction alone its
bulging fetal surface already presents at the external os. That this
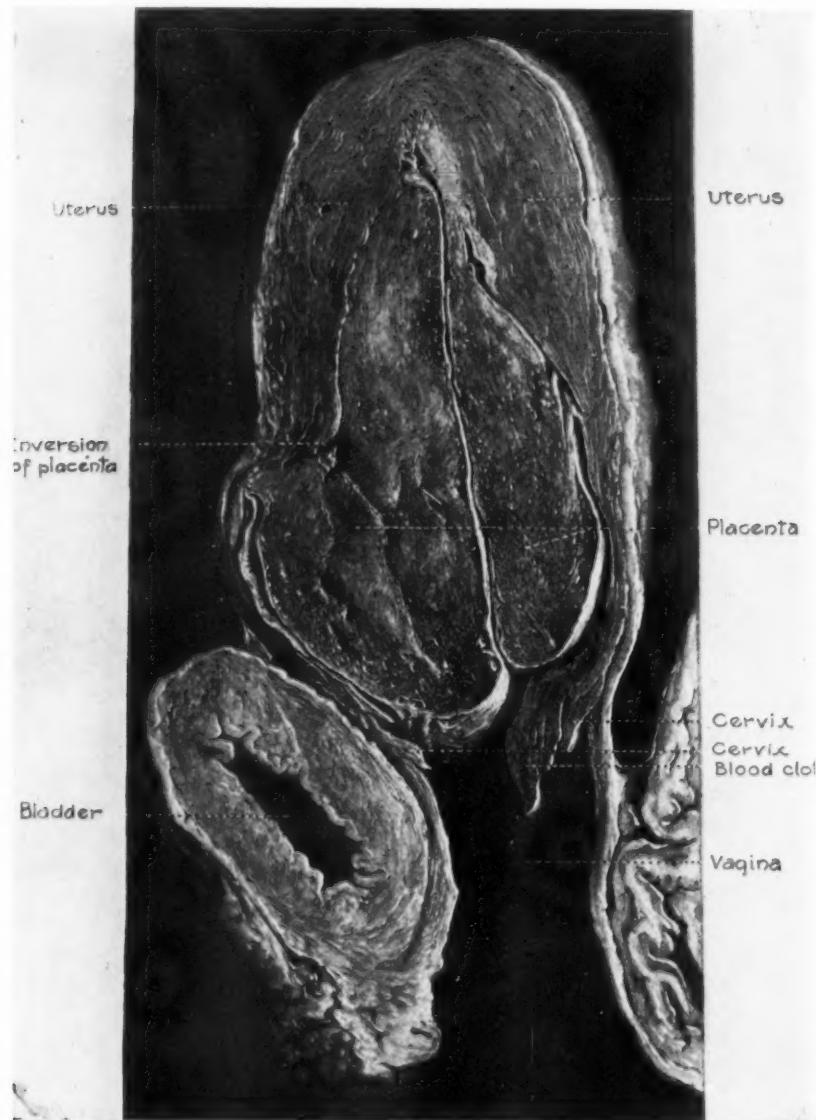
Fig. 2.—Third stage of labor. Mesial section through uterus. Placenta rolled on
itself and sectioned in such a way as to show a membranous septum, with fetal
surface presenting at external os.   Marked muscular contraction of upper portion
of uterus, lower segment still thinned out.

has been chiefly accomplished by muscular contraction is evidenced
by the fact that the fundal portion of the uterus has contracted and
foreshortened itself but unequally so, extending on the anterior sur-

face down to the circular vein which is generally conceded to locate
the contraction ring or lower edge of the upper uterine segment.
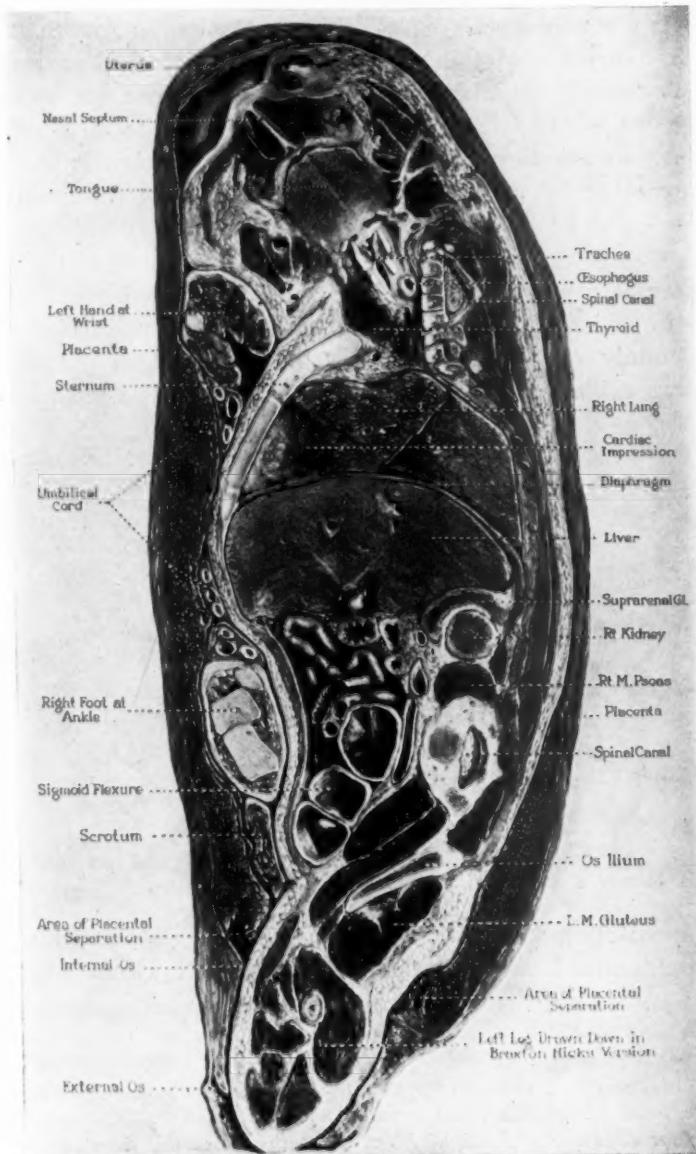
Fig. 3.—Placenta previa after version of Braxton-Hicks. Right half of uterus.
Placental attachment extends high on wall of uterus, while left leg drawn down
through cervix effectively tampons against further hemorrhage. Area of placental
separation is comparatively slight for such profuse hemorrhage.

Posteriorly, however, the contraction and thickening of the uterine
wall does not yet extend to the upper edge of the lower uterine seg-
ment, and here the separation of the placenta is still incomplete.

The inversion or infolding of the placenta with its fetal surface presenting at the external os of the cervix is clearly indicated in the drawing. The internal os cannot be identified.

Fig. 2 is a mesial section about 2.5 cm. thick. In this figure that portion of the placenta lying posteriorly, still attached at its upper end and apparently divided from the main portion by a double septum, is merely one edge of the placenta rolled round like an omelet and cut off in the sectioning. The dark mass marked below is blood clot, nor is any other intrauterine bleeding discernible in the specimen.

CONCLUSIONS

1. Placental separation, according to the so-called mechanism of Schultze in which the organ is inverted and extruded fetal surface first, is mainly accomplished by uterine contractions during third stage, comparable physiologically to those of first and second stages.
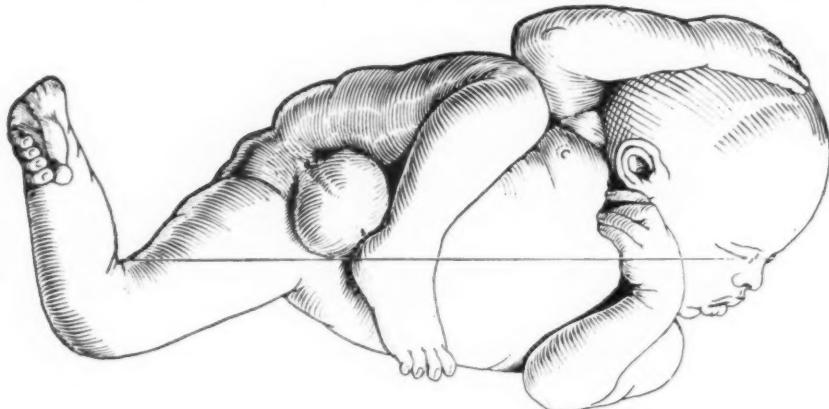
Fig. 4.—Sketch showing posture of fetus in utero after version. Line indicates direction of section through fetus, view being at right angles to that in Fig. 3.

2. In placental separation the rôle played by the supposed formation of a retroplacental hematoma has been greatly overestimated.

CASE 2.—Mrs. J. E. M. (Hosp. No. 7542-1917), a multipara aged thirty-eight, was sent to the Hospital by Dr. W. H. McCafferty of Freeport, Pa., who gave for her the following history: The patient was nearly nine months pregnant when, four days before being referred to the hospital, she had a profuse, painless hemorrhage from which she became pale and mildly shocked. During the intervening four days she bled slightly but constantly. At the time of admission she was blanched and pulseless.

The external os admitted two fingers with difficulty and the internal os was completely covered with placental tissue. This was quickly bored through and without anesthesia the combined external and internal version of Braxton-Hicks performed, the left leg being drawn down so that the knee was visible at the vulva. An intravenous injection of normal salt solution was given simultaneously but the pulse failed to return at the wrist, and three hours after admission the patient died in shock, the result of her hemorrhages.

The autopsy disclosed general anemia and pyonephritis. The pregnant uterus was removed together with part of the vagina, the specimen frozen and sectioned.
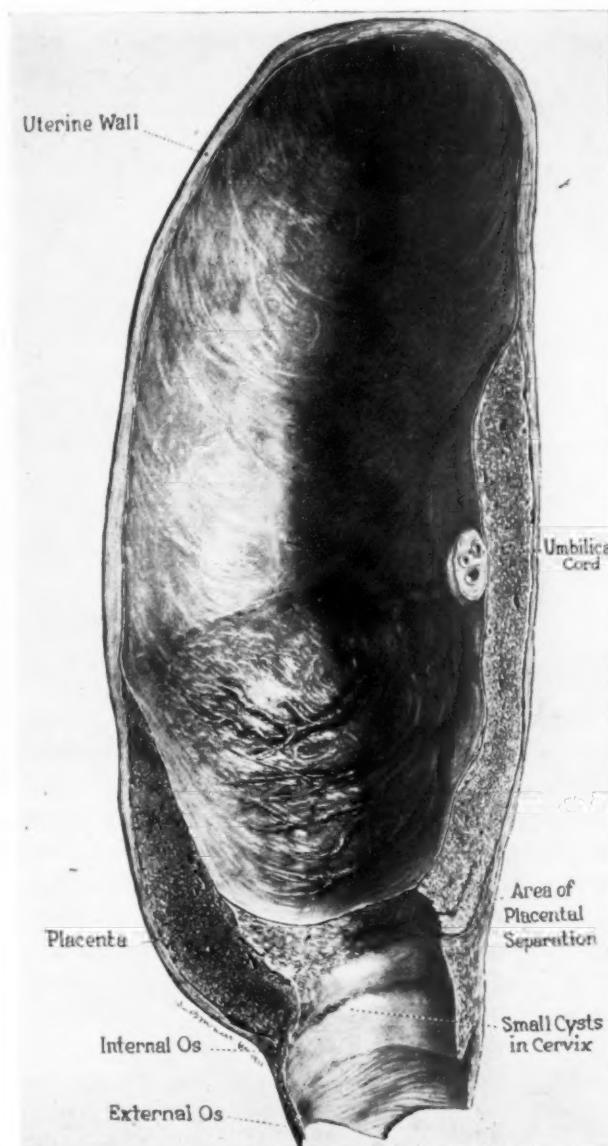
Fig. 5.—Placenta previa after version of Braxton-Hicks. Left half of uterus. Portion of sectioned fetus lifted out to show cavity of uterus with placenta attached over entire lower segment. Area of compression of placenta is seen over internal os, where thigh of fetus had been delivered to check hemorrhage from placental separation.

The illustration (Fig. 3) is self-explanatory, the outstanding features of the specimen being the size and location of the placenta, the areas

of placental separation, and the efficacy of the tamponade produced by the wedge of the thigh after version of Braxton-Hicks for placenta previa. This is the right half of the uterus.

The extraordinary height to which the edges of the central placenta previa extend up the walls of the uterus destroys the usual conception of this pathologic condition. Moreover, the apparently trifling degree of placental separation necessary for fatal hemorrhage is surprising.

The position of the fetus *in utero* after the version was such that the presenting thigh has been cut through obliquely. Fig. 4 was therefore prepared, in order that the anatomic relations noted in Fig. 3 might be clarified. This sketch shows the approximate posture assumed by the fetus after the version, the black line indicating the course of its longitudinal section, the view being at right angles to that in the preceding illustration.

Fig. 5 is a drawing of the left half of the uterus (the opposite to that shown in Fig. 3) after its portion of the fetus had been lifted out.

Here again one is surprised at the amount of uterine surface covered over by this obviously thinned out placenta. The area of placental detachment on this side is small, and the result of the pressure of dilating thigh and buttocks of the fetus on that portion of the placenta at the internal os is clearly indicated.

CONCLUSIONS

1. A central placenta previa may cover a larger portion of the uterine surface than has been generally supposed.

2. A comparatively trivial area of placental detachment may cause serious or fatal hemorrhage.

3. These sections establish the already clinically known fact that the combined external and internal version of Braxton-Hicks is an efficient method of controlling hemorrhage from placenta previa.

1015 HIGHLAND BUILDING.

TREATMENT OF PLACENTA PREVIA*

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S O much has been written, especially in the last few years, regarding the etiology, anatomy and pathology of this condition, and so many figures have been brought to our notice, that it seems hardly worth while, in presenting this subject to an audience composed of specialists, to use up the time which is necessarily short in discussing these phases of the complication.

I wish, therefore, today to present very briefly the problem of the treatment of placenta previa by the methods commonly in vogue and to see if we cannot bring out in the discussion, the ideas of the men who are seeing these cases, and by the results of their experience put the management on a more fixed basis.

In the first place, for the purpose of studying results, it seems to me that the cases should be divided in two groups: the first, those in which there is a viable child; and the second, those in which the previa is discovered so early that the possibility of a living child is not to be considered, or only secondarily.

With this broad classification approved the methods of treatment generally in vogue may be considered. The diagnosis being established by the ordinary signs and symptoms, familiar to all, the methods presenting are:—packing the lower uterine segment, cervix and vagina with gauze, leaving it *in situ* sufficiently long to cause active labor pains and dilatation of the cervix, at the same time controlling the hemorrhage; introduction of a Voorhees bag designed to accomplish the same purpose; where sufficient dilatation already exists, rupturing the membranes, followed or not as the case may warrant, by the bringing down of the leg and allowing the labor to proceed; lastly the method of abdominal section.

All of these procedures have their advocates and undoubtedly all of them have their place, but which method is to be applied to the individual case, is the problem which demands attention. A careful survey of the published figures of various authors, shows that there is a maternal mortality of from 5 to 20 per cent, with a fetal mortality ranging from 20 to 80 per cent.

In December, 1907, I presented a series of two hundred and fifty cases from the wards of the New York Lying-In Hospital in which the maternal mortality was 18 per cent and the stillbirth morality was 44.4

per cent. In the last five hundred and ninety-one cases on the same service, seventy mothers died, a mortality of 12.1 per cent; with a stillbirth mortality of about 42 per cent. A considerable improvement in the maternal mortality, but only a very slight one in that of children. Again many of the children died within the first few days, due to prematurity, for in the five hundred and ninety-one cases three hundred and seven or more than half the total, were premature.

Armin Wachter[1] quotes a maternal mortality ranging from 7.6 per cent in 1888-1907 down to 3 per cent from 1914-1918, but gives a fetal mortality of 74.8 per cent and is inclined to favor packing followed by version.

Hannal[2] favors rupturing membranes early and either allowing the head to control the hemorrhage, or doing bipolar version. He also favors cesarean section in the latter months of pregnancy.

Brodhead[3] believes that cesarean section should be done in all patients having a central previa near term where the child is viable, or in the same case even with a partial previa if no dilatation be present, quoting a maternal mortality of 15 per cent.

Boyd,[4] on the other hand, reports a series of fifty-nine cases with a mortality ranging from 7 per cent to 11.8 per cent, a fetal mortality of 79 per cent in which cesarean section was done, and therefore concludes that cesarean section should not be performed.

Hirst[5] goes into the treatment in great detail, and favors the bag and internal podalic version. He quotes a maternal mortality of 7 per cent with a fetal mortality of 60 per cent. He favors cesarean section done in the interest of the mother.

In my recent series already mentioned, the preference in treatment was given to gauze packing, followed in most instances by an internal podalic version, this being done in 354 out of 591 cases. There were 34 abdominal cesarean sections, two extraperitoneal cesarean sections, three vaginal hysterotomies, 20 Braxton-Hicks operations, 43 breech extractions and 22 craniotomies on dead children, the rest being made up of forceps and normal deliveries. The resultant mortality to the mother, as already stated, was 12.1 per cent with a stillbirth mortality of 42 per cent. One hundred and seven children, born alive, died before leaving the hospital, or about 18 per cent, a total fetal mortality of slightly over 60 per cent.

Granting that in many instances, perhaps in the greater proportion, the mothers were greatly exsanguinated on entrance to the hospital, that the children were premature or not alive when first seen, all of which conditions must necessarily prevail in a service as acute as ours, it will be well to observe from experience what seems to be the most satisfactory way of handling these cases.

No one thing has contributed more to the successful issue in placenta previa, as far as the mother is concerned, than the practice of blood transfusion, so that in all cases as soon as the diagnosis is established, the mother should be grouped as to her blood and a satisfactory donor obtained whose presence should be maintained within easy reaching dis-

tance until the necessity for his or her services is no longer needed for the patient. The factor of time in giving a transfusion is of the utmost importance, as well as that of proper technic, and it follows then, as a matter of course, that the patient should be in a well equipped hospital which in these days is practically always available.

Having made the diagnosis, *immediate treatment* should be instituted without procrastination, and one of the recognized methods of operation employed. From my experience and the reports of others, it would seem that if the patient has an undilated or slightly dilated cervix, is at term or nearly so and has a living child, that an abdominal cesarean section rapidly performed by a competent operator offers the best solution for mother and child, this applying to primipara and multipara alike. If the patient is in fair condition when first seen, and has not been infected by injudicious manipulation, the ensuing result should vary little from that of similar operation done for some other indication. If, on the other hand, the child be dead or nonviable, one of the other less drastic means of delivery may be employed, and of these in general I am inclined to favor tamponade with iodoform gauze strips. This will, in practically all instances, control the hemorrhage, especially if the membranes are first ruptured; it stimulates labor pains, causing dilatation of the cervix, stays where it is put until removed by the operator, which is not always the case with hydrostatic bags, and if applied under aseptic conditions, is, in my opinion, not as potent a source of infection as commonly believed. Iodoform is used in preference to plain gauze because it resists putrefaction longer than plain gauze, and if packed tightly rarely gives rise to iodine poisoning. The gauze should be firmly packed as far up as it will go into the uterine cavity, the cervix filled, as well as the vaginal fornices, and the vagina. Such a pack in nearly every instance thoroughly controls hemorrhage and may be left *in situ* for a considerable time without cause for worry.

When the patient has had hard contractions for some time and it is judged that the cervix is sufficiently dilated to allow the extraction of the child, she may be placed on the operating table, an anesthetic administered, under the best aseptic precautions, the packing removed and the extraction proceeded with in the manner chosen by the operator. I usually remove the placenta manually and repack the uterus. Care should be taken not to handle the cervix more roughly than necessary, as in these cases it is very friable and more apt to tear, thus promoting hemorrhage and subsequent infection. A transfusion should be ready at the time of delivery and if there is any doubt at all of its necessity, it should be given without delay. Pituitrin and ergot may be used after delivery and uterine packing to aid in contracting the uterus.

I believe that most of the maternal mortality in placenta previa is

due to delay in diagnosis of the condition, accompanied by tardiness in treatment, combined with careless manipulation and resultant infection, all of which are preventable and inexcusable. If these factors are eliminated, as they can be, the results for the mother should be much improved and a patient will rarely be lost. Regarding the fetal mortality, so much cannot be said, as the greater majority of the children are so premature that little can be done to save them even if born alive. Cesarean section on the viable fetus, does offer a means of lowering this mortality to an appreciable degree and should be employed in this class of cases more frequently.

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125 EAST THIRTY-NINTH STREET.

THE URIC ACID CONTENT OF HUMAN AMNIOTIC FLUID

BY J. LISLE WILLIAMS, M.D., AND J. A. BARGEN, M.D., EVANSTON, ILL.
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IN his comprehensive studies of the physical and chemical properties of human amniotic fluid Uyeno[1] demonstrated the presence of uric acid, but was unable to estimate the amount. Apparently this is the only instance mentioned in the literature regarding either the presence or amount of uric acid in human amniotic fluid. Previously Amberg and Rowntree[2] had discovered that creatinine is a normal constituent.

The improvement in methods for the quantitative estimation of the nonprotein nitrogen constituents of body fluids has made possible their accurate determination in the amniotic fluid. These substances as well as the amount of the sugar and chlorides and the carbon dioxide combining power were determined quantitatively. The amniotic fluids of twenty women were examined, eleven of whom were normal and nine were from patients abnormal in some way. The fluid was obtained by aseptic puncture of the fetal membranes during labor or in two instances from the uterine cavity after hysterectomy. Chemical analysis was started immediately or after a few hours' refrigeration. Owing to the obvious impossibility of obtaining all the fluid during labor no attempt was made to measure all the fluid present. The amount of fluid actually obtained varied from 19 to 590 c.c. Except

in one patient with hydramnios the amount did not appear to exceed the normal.

The methods of Folin and Wu[3] were used for the determination of the sugar and nonprotein nitrogen substances, that of Austin and Van Slyke[4] for chlorides and that of Van Slyke and Cullen[5] for the carbon dioxide combining power. A check on the method for sugar in the amniotic fluid was made by using the method of Benedict and Osterberg[6] for sugar in normal urine and the comparative results were satisfactory.

The results of these studies are collected in the following tables. In Table I are the figures from the amniotic fluids of eleven normal women; in Table II the results from nine abnormal women.

TABLE I

NO.	SUGAR %*	UREA N*	TOTAL N-P-N*	URIC ACID*	CREATININE†	CHLORIDE*	CO₂‡
1	.017	17.00	23.70	6.71	1.96	5.93	37.63
2	.014	16.77	27.17	4.49	1.89	5.20	26.92
3	.022	10.51	21.27	1.99	1.64	6.66	
4	.035	18.04	22.67	1.93	1.70	6.02	
5	.021	21.29	33.56	4.75	1.92	5.52	
6	.000	20.55	31.26	4.61	2.28	6.51	39.01
7	.021	18.87	26.60	4.05	3.95	6.05	30.39
8	.014	26.95	33.71	6.46	2.49	5.70	36.35
9	.011	17.18	25.74	2.52	2.03		
10	.020	11.34	16.22	4.33	2.15	6.33	39.30
11	.021	22.31	35.45	7.73	3.61	5.39	33.83
Av.	.0196	18.25	27.05	4.51	2.33	5.93	34.77

TABLE II

NO.	SUGAR %*	UREA N*	TOTAL N-P-N*	URIC ACID*	CREATININE†	CHLORIDE*	CO₂‡
1	.0205	27.00	36.82	5.51	2.40	5.82	27.64
2	.017	11.98	20.98	2.93	2.01	6.25	37.36
3	.013	12.17	16.26	3.54	1.96	6.09	34.88
4	.000′	49.74	75.96	8.51	2.73		
5	.025	15.04	19.47	1.94	1.25	6.33	29.27
6	.000	13.44	23.71	5.20	2.19	6.37	37.90
7	.019	18.93	26.13	2.19	2.14	5.99	31.00
8	.033	40.58	55.23	2.46	6.66	6.99	32.35
9	.025	11.91	17.90	1.98	1.35	6.48	28.77
Av.	.017	22.53	32.49	3.81	2.52	6.28	32.39

*mg. per 100 c.c. of fluid.
†gm. per liter of fluid.
‡gas in volumes per cent.

DISCUSSION

The results listed in the tables demonstrate that both uric acid and creatinine are present in the amniotic fluid of pregnant women in measurable amounts. The concentration appears not to vary in relation to any particular pathologic condition although the highest value, 8.51 mg. per 100 c.c., was present in the fluid of a patient with the toxic vomiting of pregnancy. However, as the normal women ap-

proached the termination of their pregnancy, the concentration of uric acid appears to increase and the highest value, 7.73 mg., was obtained from a patient three weeks overdue.

Included in Table I are the results obtained from the fluids of five women whose pregnancy terminated from three days to three weeks before term, and six in whom labor was delayed for three days to one month after the expected time. In the latter group the averages for urea, total nonprotein nitrogen and uric acid are about 40 per cent higher than in the former. Th averages for creatinine, chlorides and the CO_2 combining power are approximately the same. The values obtained for urea, nonprotein nitrogen and chlorides agree fairly well with those published by Clogne and Reglade[7] and Labat and Favreau.[8] This fact supports the theory that the amniotic liquid at term may consist partially of fetal urine. The observations of Labruhe[9] are in accord with this view.

In the amniotic fluid of three patients with hypertension or pre-eclamptic toxemia the average amount of uric acid is 3.99 mg. per 100 c.c. as compared with 4.51 mg. for that of the normal patients. Age, race and the number of pregnancies have no appreciable effect upon the concentration of any of the organic or inorganic constituents studied.

Uyeno[10] found no sugar but demonstrated d-lactic acid as a constant component. Labat and Favreau[11] examined six fluids and demonstrated 0.1 per cent dextrose in one. With the method here employed all but three fluids contained sugar in measurable quantities.

In hydramnios Prochownick and Harnack[12] found the amount of urea and creatinine increased. The values reported here for one patient with hydramnios are essentially the same as the average for normal women.

Observations on both blood and amniotic fluid were made simultaneously on five women and in every patient the concentration of uric acid in the amniotic fluid was higher than in the blood; the average amount in the amniotic fluid was 5.29 mg., in the blood 3.60 mg. per 100 c.c.

CONCLUSIONS

1. Uric acid and creatinine are demonstrable in human amniotic fluid by Folin's methods and exist in a concentration greater than in the blood.

2. The reducing sugars in the amniotic fluid can be estimated by the method of Folin and Wu, the concentration normally averaging about 0.02 per cent.

3. The amount of urea, nonprotein nitrogen and uric acid in human amniotic fluid increases as the term of pregnancy is prolonged.

4. The capacity of the amniotic liquid to combine with CO_2 is considerably less than that of normal blood.

5. The increase of the nonprotein nitrogen in the amniotic fluid in advanced pregnancy suggests that the fetal urine may be a partial source of the liquid.

6. The greater concentration of uric acid in the amniotic fluid over that in the blood suggests that in the toxemias of pregnancy the increased uric acid of the blood may arise in part from a more highly saturated amniotic fluid.

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URIC ACID IN THE BLOOD IN THE TOXEMIAS OF PREGNANCY

By E. L. KING, M.D., and W. DENIS, Ph.D., NEW ORLEANS, LA.

(From the Department of Obstetrics and the Laboratory of Physiological Chemistry of the School of Medicine, Tulane University.)

ABOUT two years ago Williams[1] published the results of a series of observations on the blood of pregnant women suffering from various types of toxemias, as a result of which he was led to the conclusion that in the blood of patients with eclampsia, hyperemesis gravidarum, and with the symptoms of preeclamptic toxemia together with arterial hypertension, the uric acid is markedly increased, that on delivery and recovery this constituent of the blood of such patients declines to a normal figure, and finally that the toxic vomiting of pregnancy is associated with an increase in the uric acid in the blood, whereas the nervous or physiologic vomiting is not. Shortly after the appearance of Williams' paper, Caldwell and Lyle[2] and Killian and Sherwin[3] published the results of extensive series of observations on the nonprotein constituents of the blood of normal pregnant women and of patients suffering from toxemias of various types, and reported that in many of these latter cases notable increases in blood uric acid were found.

TABLE I

URIC ACID IN THE BLOOD OF NORMAL PREGNANT WOMEN

CASE NO.	AGE	GRAVIDA	GESTATION MONTH	MG. PER 100 C.C.	
				NONPROTEIN NITROGEN	URIC ACID
36	20	II	2.0	27.6	2.0
49	18	I	2.0	29.2	3.2
62	18	I	2.0	21.7	2.4
42	22	II	3.0	22.6	2.1
40	31	IV	4.0	24.5	2.7
63			4.0		
1	25	I	4.0	25.5	2.9
3	21	I	4.0	25.0	2.8
5	17	I	4.0	25.4	2.9
23	30	III	5.0	22.6	1.9
26	18	I	5.0	20.8	2.1
2	27	III	6.0	24.0	2.8
4	24	II	6.0	29.8	2.7
7	25	VI	6.0	31.2	2.6
9	22	III	6.0	29.4	2.8
51	19	II	6.0	22.2	2.9
60	18	II	6.0	22.2	2.1
29	22	I	6.0	24.0	2.1
6	18	I	7.0	24.1	2.8
16	19	I	7.0	30.6	3.0
17	22	I	7.0	28.1	2.9
19	17	I	7.0	24.5	2.8
20	37	IX	7.0	25.7	2.6
24	23	I	7.0	25.5	2.8
31	38	II	7.0	25.5	2.4
35	18	I	7.0	26.0	2.5
41	17	I	7.0	27.2	2.5
44	23	IV	7.0	29.9	3.0
48	20	II	7.0	24.9	2.5
53	35	VIII	7.0	23.5	2.3
56	19	I	7.0	24.9	2.16
55	22	I	7.5	23.5	3.3
46	16	I	7.5	24.6	2.2
33	17	I	7.5	23.1	2.3
11	19	I	8.0	23.0	2.5
12	37	VIII	8.0	21.8	2.2
13	17	I	8.0	28.5	2.7
16	24	I	8.0	24.0	2.6
22	30	VI	8.0	25.7	2.2
25	20	I	8.0	22.21	2.4
27	21	IV	8.0	27.2	2.7
28	18	I	8.0	22.9	2.1
32	25	V	8.0	23.0	1.9
38	21	I	8.0	24.4	2.1
39	18	I	8.0	24.9	2.7
43	15	I	8.0	21.4	2.5
45	24	III	8.0	23.5	3.0
52	21	II	8.0	20.3	2.1
54	21	II	8.0	24.9	2.5
58	22	II	8.0	20.3	2.1
59	20	I	8.0	25.5	3.3
47	18	I	8.5	24.9	3.2
8	37	VI	9.0	30.	3.2
14	21	I	9.0	21.4	2.5
15	22	II	9.0	29.2	3.1
18	23	IV	9.0	25.7	2.9
21	18	II	9.0	21.8	2.0
30	23	III	9.0	29.6	2.6
34	25	II	9.0	26.6	3.2
37	21	I	9.0	23.5	2.5
50	27	III	9.0	30.7	3.2
57	17	I	9.0	22.6	3.2

TABLE II

URIC ACID IN THE BLOOD OF PATIENTS SUFFERING FROM VARIOUS TYPES OF TOXEMIAS
OF PREGNANCY

CASE NO.	DATE	MG. PER 100 C.C.		HISTORY
		NON-PROTEIN NITROGEN	URIC ACID	
5	7/ 9/21	25	8.1	A multipara, age 40 years, had 2 convulsions and died 12 hours after admission. Had been under treatment for albuminuria and hypertension. Blood sample taken shortly before delivery.
24	8/18/21	33	6.5	a) A primipara, 19 years old, colored, admitted in labor, 3 convulsions after admission, delivered in 75 minutes, had been edematous for 4 to 5 weeks, but without toxic symptoms. Blood taken on day of delivery.
24	8/26/21	28	5.1	b) Convalescent, urine still shows albumin.
24	8/30/21	25	5.0	c) This sample taken just before patient was discharged from the hospital. Urine still shows albumin.
30	8/26/21	32	4.6	A multipara, age 22 years, slight edema for 4 months, normal delivery 2¾ hours after admission. B.P. systolic, 220. Urine showed a large trace of albumin and many casts. Recovery, but with persistent hypertension. Blood sample taken the day after delivery.
39	10/23/21	24	7.6	A primipara, age 21 years, edema for one week with some toxic symptoms with 1 convulsion 16 hours before labor was induced. Blood sample taken shortly before labor.
39	11/ 3/21	39	5.6	The second sample was taken shortly before discharge, at which time the patient still showed hypertension and albuminuria.
42	11/ 9/21	33	5.0	A multipara with a history of 2 normal pregnancies. Marked albuminuria and hypertension. Labor induced 11/14/21.
42	11/29/21	35	3.9	At this time, although the patient's condition was good, albuminuria still persisted.
43	11/29/21	130	10.2	A multipara, with a history of previous normal pregnancies admitted in coma, 4 convulsions in 8 hours, 1 convulsion 1 hour after cesarean section. Blood taken before delivery.
43	12/16/21	100	10.1	Convalescent. Urine still contains a large trace of albumin. B.P. Systolic, 190.
45	11/29/21	30	3.0	A multipara, hypertension and albuminuria, normal delivery 12/10/21, recovery.
46	11/29/21	60	10.2	A multipara, age 44. Urine shows much albumin and many casts. Delivered of a stillborn child (macerated) 3 days after the sample of blood was taken. Recovery.
56	2/ 9/22	62	4.4	Primapara, age 18 years, urine showed albumin and casts, labor induced. Died.
49	12/10/21	75	6.6	A multipara, age 26 years, admitted in coma, several convulsions in 10 hours, delivered a few hours after the sample of blood was taken. Died.
53	2/ 2/22	32	5.0	A primipara, 18 years old, general edema, urine shows a large trace of albumin and a few casts. Delivered 2/29/22. Recovered.
54	2/ 2/22	28	2.5	A primipara, albuminuria, and slight toxic symptoms on admission. Delivered 2/26/22. Recovery.

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23	30	III	5.0	22.6	1.9
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4	24	II	6.0	29.8	2.7
7	25	VI	6.0	31.2	2.6
9	22	III	6.0	29.4	2.8
51	19	II	6.0	22.2	2.9
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6	18	I	7.0	24.1	2.8
16	19	I	7.0	30.6	3.0
17	22	I	7.0	28.1	2.9
19	17	I	7.0	24.5	2.8
20	37	IX	7.0	25.7	2.6
24	23	I	7.0	25.5	2.8
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35	18	I	7.0	26.0	2.5
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30	8/26/21	32	4.6	A multipara, age 22 years, slight edema for 4 months, normal delivery 2¾ hours after admission. B.P. systolic, 220. Urine showed a large trace of albumin and many casts. Recovery, but with persistent hypertension. Blood sample taken the day after delivery.
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43	11/29/21	130	10.2	A multipara, with a history of previous normal pregnancies admitted in coma, 4 convulsions in 8 hours, 1 convulsion 1 hour after cesarean section. Blood taken before delivery.
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49	12/10/21	75	6.6	A multipara, age 26 years, admitted in coma, several convulsions in 10 hours, delivered a few hours after the sample of blood was taken. Died.
53	2/ 2/22	32	5.0	A primipara, 18 years old, general edema, urine shows a large trace of albumin and a few casts. Delivered 2/29/22. Recovered.
54	2/ 2/22	28	2.5	A primipara, albuminuria, and slight toxic symptoms on admission. Delivered 2/26/22. Recovery.

About two years ago, we were led by the observations contained in Williams' paper to make a collection of results of uric determinations in the blood of normal pregnant women and of patients with various toxemic conditions, with a view to testing out the diagnostic and prognostic value of uric acid determination in the blood in such conditions. The earlier determinations of uric acid, and all of the nonprotein nitrogen figures were obtained by the methods of Folin and Wu;[4] the revised uric acid method of Folin[5] was employed in all the later analyses. Our blood samples were obtained from the out-patient clinic and the obstetric wards of the New Orleans Charity Hospital. In Table I are presented the results obtained on the blood of 62 normal pregnant women, in which collection examples of early, late and middle pregnancies are represented.

In these cases the lowest uric acid value obtained was 1.9 and the highest 3.2, while the great majority were between 2.2 and 2.5 milligrams per 100 c.c.,—values which are well within normal limits. As far as could be determined parity, age and the stage of gestation were without demonstrable effect on the concentration of the blood constituent.

In Table II are collected the results obtained on eleven cases of eclamptic and preeclamptic toxemia. In these cases an attempt was made to obtain a sample of blood before delivery, and one or more samples after delivery and during convalescence; but in many of the patients this was not possible, so that in a number of cases our observations are limited to a single analysis.

Our results may be considered as a confirmation of the observations of Williams, of Caldwell and Lyle, and of Killian and Sherwin regarding the accumulation of uric acid in eclamptic and preeclamptic toxemias, although we feel unable, either from a study of the clinical manifestations, or from an analysis of the blood to make (without the assistance of an autopsy) a differential diagnosis between hepatic and renal toxemias as have the latter investigators.

We believe that the determination of blood uric acid promises to be of considerable value in diagnosis and prognosis in eclamptic and preeclamptic conditions. Our experience has been that in preeclamptic toxemias the increased blood uric acid may serve as a useful test in doubtful cases. In our rather short series of cases we have invariably found that the more severely toxic patient showed extremely high uric acid values, a condition which was associated with little or in most cases a relatively small rise in the nonprotein nitrogen, and in cases of recovery with a relatively slow decline towards normal values. We therefore believe we are justified in making the statement that after a sufficient time has elapsed to allow for the collection of

adequate data it may be found that this determination may prove of at least equal value with the clinical tests now in use.

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512 HIBERNIA BUILDING.

HEPATITIS IN ITS RELATION TO INFLAMMATORY DISEASE OF THE ABDOMEN: A CLINICAL AND LABORATORY STUDY*

BY CHARLES GORDON HEYD, A.B., M.D.; WARD J. MACNEAL, PH.D., M.D.; JOHN A. KILLIAN, M.A., PH.D., NEW YORK, N. Y.

CLINICAL DISCUSSION (DR. HEYD)

IN considering hepatitis[1] we shall define that form of hepatitis that is associated with, or sequential to, the more chronic inflammatory diseases of the abdomen, particularly those affections involving the right upper quadrant and the appendix. Abscess, infarct, and embolism of the liver as complications of suppurative conditions, either in the abdomen or elsewhere, are not included. We refer specifically to the low grade inflammatory changes in or about the small bile radicals, the interlobular septa, the periportal veins and intrinsic degeneration of the hepatic cells.

We have recognized for a number of years a cholecystic toxemia[2] which manifests itself by changes in organs quite remote from the liver. During this period of time we have also been impressed with the macroscopic picture of the liver in patients operated upon for chronic disease of the biliary tract. There was a well founded idea that many of these cases show definite liver changes, either subsequent to infection of the gall-bladder or coincident with gall-bladder infection. From time to time in checking up our after-results we have been impressed with the clinical fact that those patients who showed gross demonstrable changes in the liver at laparotomy were those least benefited by surgery. We are convinced that there are certain types of liver change that are associated with chronic abdominal infection, and which render the patient somewhat of an invalid even after successful surgical intervention.

Peterman[3] reported that in 130 unselected cases of gall-bladder disease admitted to the surgical service of Barnes Hospital, St. Louis, Mo., there were 82 cases of undoubted liver involvement. Of these 69 were "enlarged" or "edematous," five showed adhesions alone and eight were "atrophic" or scarred. We[4] have drawn attention to the fact that at autopsies made on patients suffering from simple gastro-duodenal ulcer there were always present more or less advanced hepatic lesions. MacCarty and Arnold Jackson[5] stated that in a series of 58 cases studied in relation to hepatitis 81 per cent showed chronic inflammation. The livers were studied independently of any knowl-edge of the condition of the gall-bladder. Peterman, Priest and Graham[6] regularly produced experimental cholecystitis by injection of organisms into the lumen of the gall-bladder after ligation of the cystic duct and vessels. An associated hepatitis was invariably found associated with the cholecystitis.* Fuetterer[7] was able to recover bacteria injected into the portal vein two minutes later in the bile. Charcot (quoted by Ehret and Stolz[8]) produced biliary tract inflam-mation and later cirrhosis of the liver with marked hepatic changes by ligation of the common bile duct in rabbits and guinea pigs. Adami has demonstrated that under normal conditions colon bacilli may be pres-ent in the blood stream and eliminated from the liver in apparently normal bile. It is doubtful, however, if bacteria can pass through a normal liver on account of the high bactericidal power possessed by the liver tissue. It would appear more probable that there must be some inflammatory changes in the liver itself to allow bacteria to traverse the liver substance. An injection of microorganisms in the appendiceal vein is followed by hepatitis and cholangitis while surgical infection of the liver by way of the portal system has its clinical pathology well demonstrated in the septic pyelophlebitis following gangrenous appendicitis.[9] This is essentially an acute septic process and a mechanism of liver injury with which we are not concerned at this time.

Werelius[10] in discussing high intestinal obstruction has brought for-ward experimental evidence that in all drained duodenal loops bile secretion stops before death. It is possible that with the cessation of biliary secretion the other hepatic functions are simultaneously termi-nated and death is the result of liver insufficiency. As a corollary, the liver insufficiency is directly due to liver exhaustion following the absorption of the toxic substances which accumulate within the lumen of the obstructed gut.

The question naturally suggested is, what is the route by which the liver is injured in these cases. There is no anatomic connection be-

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*Nine out of the nineteen experimental dogs died of a general peritonitis. The hepatitis might possibly be due to the peritonitis rather than the cholecystitis.

tween the arterial blood of the gall-bladder and liver, the only canalic-
ular system common to both organs in the lymphatic system.   There
is also no anatomic route from the appendix to the gall-bladder ex-
cept through the intermediate agency of the portal system and the
liver. The liver may be infected presumably in five ways: (1) hematog-
enous infection; (2) by means of the portal system; (3) through the
lymphatics and (4) from contact with contiguous pathologic organs;
(5) ascending infection by way of the bile ducts.

We have extended our study to the microscopic examination of
specimens of liver removed during the course of operations for acute
and chronic appendicitis, ulcer, and carcinoma of the stomach.   In
a few traumatic cases we have studied the liver for purposes of ob-
taining a normal control.   The observations were made preponderantly
in cases of gall-bladder disease.   It has been our custom, however, to
remove the appendix through a high right rectus incision and ad-
vantage has been taken to study the liver in the course of operations
for acute and chronic appendicitis, as well as all pathologic conditions
affecting the gastroduodenal segment.   The study, so far as the liver
itself was concerned, embraced a careful inspection of the liver in
regard to: (1) size, shape, deformities, disproportion in lobes, changes
in color as well as differences in the color, contour and texture be-
tween the right and left side of the liver; (2) the character of the
anterior border with estimation of friability; (3) the presence of
crenation, retraction and dimpling of liver tissue; (4) changes in the
surface of the exposed portion of Glisson's capsule, the presence of
subscapular infiltration, fibrous tissue replacement, adhesions, stellate
cicatrices, wrinkling of liver surface, opacity of Glisson's capsule with
infiltration or thickening of falciform or round ligament and fibrosis
at umbilical notch,—in short, partial or complete Glissonitis; (5) the
presence of adhesions about the gall-bladder and central fissure, an
increase in fibrous elements about the gall-bladder notch, widening
of area of opacity on either side of gall-bladder by fibrous tissue re-
placement, etc.

It has been our custom to remove two to three pieces of liver tissue
in each case.   The first section removed was usually from the neigh-
borhood of, or adjacent to, the gall-bladder, the second piece from the
superior surface of the right lobe and about 5 cm. distant from the
gall-bladder, and less frequently from the superior surface or anterior
border of the left lobe, depending upon the accessibility of this por-
tion of the liver.   It may be stated that when we found macroscopic
liver changes present these pathologic changes were uniformly dis-
tributed throughout the right lobe of the liver, and at the same time
there was always evidence of the same pathologic process in the left
lobe but ordinarily of less intensity than in the right lobe.   It occa-

sionally happened that the liver changes were much more marked than the associated pathology in the gall-bladder, appendix or stomach. In other words, the changes in the abdominal viscera were quite minimal as compared to those encountered in the liver. Insofar as the gall-bladder was concerned as an etiologic factor in hepatic change it did not seem to make much difference whether stones were present or absent. The essential elements were apparently: (1) chronicity of the infective processes; (2) the persistence of a certain degree of intensity of the offending agent—chemic or biochemic. In catarrhal types of appendicits and cholecystitis the evidence obtained from inspection of the liver consisted in a thickening of the capsule, with occasional adhesions, with thickening of the anterior border, with crenation, swelling and surface dimpling. In localized gall-bladder disease the changes in the area of the gall-bladder region were more intense than elsewhere, and the quality of the change varied inversely with the distance from the gall-bladder. In these cases the microscopic examination of the liver section would show subscapular lymphocytic infiltration and intercellular lymphatic infiltration. If there were an acute inflammation in the appendix or gall-bladder disease, leucocytic infiltration would be merged with lymphocytic infiltration. When the abdominal condition was essentially chronic the surface changes on the liver would become more marked and more diffuse, together with an increase in the size of the liver. The liver was grossly enlarged in about 50 per cent of the cases and the enlargement when present was confined in about 90 per cent of the cases to the right lobe and particularly the outer and posterior half of the right lobe—the quadrate and caudate lobes not participating in gross enlargement. Microscopically the liver changes in the more chronic cases represented an advance in pathologic intensity with the chronicity of the abdominal condition. Uniform fibrosis was more marked, loose connective tissue would be found in abundance about the bile ducts and portal veins, bile stasis would be more apparent with hyperplasia and budding of immature bile ducts. Leucocytic and lymphocytic infiltration would extend between flattened and distorted liver cells. Many of the latter would show vacuoles and disintegration, occasionally intra- and intercellular pigment, with some fatty degeneration and hepatic cell destruction, rarely hyperplasia of blood capillaries and an increase in syncytial cells of Kupffer. Apparently, so far as we could observe, there was no definite parallelism between the gross and qualitative liver changes and the pathologic condition of the associated abdominal condition. In some cases it was apparent that the force of the affection was spent on the originally infected viscus remote from the liver; in other cases the force of the offending agent apparently exerted its greatest injury on the liver with

minimal changes in the extrahepatic viscus which many times was showing a well established repair.

The liver [11], [12] is a complete biochemic laboratory which, interposed between the portal and systemic circulation, transmutes the food into energy value. It is the chief of the metabolic work shops and regulates body metabolism by enzyme action. Some of the enzymes are intrinsic and elaborated by the liver itself and others are extrinsic and brought to it from different viscera by the circulation. Hess and Serege[13] ascribed various functions to different portions of the liver. It is interesting to recall that Silvestri[14] and others attempted to specialize liver function in regard to the right and left lobes of the liver. It has been a frequent observation that when the liver is enlarged in diabetes the right lobe is more uniformly affected, while in Banti's disease and other splenomegalias it has been observed that the left lobe participates more particularly, while tropical liver abscess is almost exclusively on the right side. The work of Glenard and Serege lends emphasis to this contention for in their experiments the left lobe of the liver is intimately connected with the stomach and spleen, while the right exhibited more definite relationships with the pancreas and small intestine, and the ordinary form of interstitial cirrhosis manifests itself most markedly on the left side. The injection of staining fluids into the spleen invariably produced discoloration of the liver limited to the left lobe while injections into the superior mesenteric veins, as a rule, stained the right lobe of the liver more than the left.[15]

The liver has an unusual vascular supply, an arrangement of afferent and efferent blood that is found in no other organ in the body.[16] The spleen and kidney perform their specific functions in the presence of a large supply of oxygenated blood. The liver, to the contrary, performs its functions with a blood that, except for a relatively very small amount of arterial blood supplied by a minor portion of the hepatic artery, is entirely of a venous type. Two-thirds of the arterial blood via the hepatic artery is diverted to the gastroduodenal, pyloric, supraduodenal and cystic arteries. One has only to compare the arterial blood of the liver with the arterial blood sent to the spleen or kidney, the latter two organs performing their functions in the presence of an adequate or ample oxygenated blood. The liver, on the contrary, performs all of its functions upon the blood that is essentially nonoxygenated, as the liver cells receive blood only from derivatives of the portal vein, the hepatic artery supplying the walls of the blood vessels, the bile ducts and the liver capsule. It has not been definitely demonstrated whether any of the hepatic arterial blood goes beyond the interlobular septa; such transference of material from arterial blood to hepatic cells must

be by osmosis and not by anatomic arterial canaliculi as the hepatic artery has no paralleling veins. Again, the venous blood entering the liver is diverse in its source and different in quality from ordinarily considered venous blood. The portal blood represents (1) from one-sixth to one-eighth of the splenic venous blood, deprived of most of its oxygen after passage through the spleen; (2) the mesenteric venous blood is surcharged with products of absorption from stomach, duodenum, pancreas, small intestine and the major portion of the large intestine. On the other hand, the hepatic veins carrying the blood from the liver to the vena cava, in addition to the above moities, has the venous equivalent of the hepatic arterial blood.

The functions of the liver are diverse and obscure but certain activities may be predicated at this time. The liver concerns itself with (1) the maintenance of a proper blood sugar level through the glycogen metabolism.[17, 18] In this activity there is apparently a reciprocal relationship with the pancreas.[19] (2) The metabolism of protein as evidenced in the formation of urea, purin and amino-acid metabolism and the ammonia balance; (3) the metabolism of facts— the liver acting as a reservoir for fat storage; (4) the secretion and excretion of bile. In this connection its activity is manifested as a filter capable of removing broken down cellular detritus coming from the spleen; (5) elaboration of fibrinogen; (6) depurative function in destroying biotic elements and detoxifying biochemic or gastrointestinal deliterants.

The liver possesses marked regenerative properties. Since every liver cell is identical with its fellow it follows that there is no specialization of special cell groups for varied or specific purposes. Each cell the moment it is fully formed can function with all its properties. No other organ in the body exhibits such pronounced regenerative capacity. The rate of the repair of the liver is so rapid that fully 800 grams of liver grows in seven to nine days.[20] Mann[21] was able to excise 70 per cent of the liver with complete regeneration within a few months, the regeneration being so rapid and ample that there was no liver deficiency produced. In addition, a sufficient number of bile ducts could be ligated so that 70 per cent of the biliary secretion was occluded without any impairment of liver function. The ligated portions of liver tissue undergoing connective tissue deposition and producing the histologic picture of biliary cirrhosis while the unligated portion of the liver underwent hyperplasia and regeneration so that hepatic function was undisturbed. MacMaster and Rous[22] have determined that three-quarters of the ducts of the liver substance in dogs and monkeys can be obstructed without pigment or cholate accumulation and that tissue icterus did not result when nineteen-twentieths of the liver substance was placed in stasis.

Under stress of additional work other viscera undergo hypertrophy : the liver, however, makes up for deficiency of function by hyperplasia —a biologic characteristic preserved by no other organ in the human body. Any liver degeneration brought about by any offending agent induces two distinct changes in the liver. The one is fibrous tissue replacement, the other hepatic hyperplasia with compensatory degeneration.[23] Widal[24] contends that the liver exerts marked protopexic functions in its ability to transform peptones—proteoses and disintegrating protein substances being found in the portal circulation during digestion. In the failure of this function there would escape into the general circulation some of these materials, producing a Crise Hémoclasique, a syndrome due to a disturbance in the colloid balance of the blood and characterized by leucopenia, fall in blood pressure, increased blood coagulability and diminution in the refraction index of the blood serum. The application of this idea to clinical medicine suggested itself as a test for liver deficiencies, in that it would seem probable that the protopexic function would be diminished in liver disease and various hepatopathies might be clinically estimated by the loss of this function. "In the few instances of sudden death following Talma operation Kretz attributed the fatal outcome of the sudden flooding of the circulation with substance which otherwise would have been detoxified in the liver. These deaths must, therefore, be considered analogous to those that occurred in Eck fistula in dogs."[26]

Central necrosis of the liver is in some way related to pancreatic activity. A liver injured in some way seems to be hypersensitive to trypsin and clinically we have found the coexistence of central necrosis and pancreatic fat necrosis, a condition that has also been observed experimentally. According to Fischler[27] death in central necrosis of the liver results from a flooding of the circulation with liver biproducts due to the action of trypsin and represents a death from split protein intoxication.

In studying the collective work of the abdominal surgeons* at the New York Post-Graduate Hospital in connection with gall-bladder surgery we were early impressed with a series of deaths and complications that could in no way be attributed to the factors that ordinarily produce death in this class of surgery. The character of these mortalities or some of the complications which ensued and did not result in death led us to believe that there was a gross disturbance in the protective function ordinarily exerted by the liver. We began to study these cases with greater care from the clinical and biochemic standpoint as well as the occasional necropsy findings.

*Services of Dr. John F. Erdmann, Dr. Edward W. Peterson and Dr. Charles Gordon Heyd.

One ordinarily expects that when a mortality follows an operation upon the external biliary passage that it would be associated with the development of shock, hemorrhage, cholemia, gastric dilatation and later possibly the development of peritonitis, the latter being the most infrequent lethal complication.

Eliminating the deaths that might be properly attributed to any or all of these causes there still remained a small group of mortalities that could not be explained upon the basis of any one of these causative factors. We have been careful to eliminate the possibility of renal complications and in the case groups about to be reported this factor was not present, as the preliminary urinary and blood study had assured us as to the physiologic competency of the kidneys before operation. However, with the development of "hepatic insufficiency" there was manifest the blood and urinary findings highly suggestive of an acute irritative nephritis. These cases represented apparently properly selected individuals capable of sustaining the traumatism of a laparotomy. They all exhibited manifest disease of the gall-bladder or external biliary passages, or of the appendix or of ulceration or cancer of the gastrointestinal tract. We have been able roughly to classify three main types[28, 29] of clinical conditions that have occasionally followed laparotomy directed to the cure of pathologic affections of the abdomen. The first type presents a clinical picture of a postoperative vasomotor depression of an extreme degree and occurring too late to be interpreted as surgical shock. The patient ordinarily has been behaving quite as usual following an operation of cholecystectomy or drainage of the common duct. At the end of twenty-four to thirty-six hours, without any apparent reason, the patient passes into a pronounced state of vasomotor collapse, with cold, clammy extremities, wet, moist and leaking skin, a very much stimulated mentality and a facial expression not unlike the facies of fear. The condition is not associated with dilatation of the stomach and there has been ample evidence of kidney function. The intravenous administration of a ten per cent solution of glucose, 1000 c.c., every four to six hours, and continuous Murphy proctoclysis with tap water has usually brought about a recovery. It is interesting to note that when this type of complication occurs it has usually been in cases that have had a previous operation upon the gall-bladder, and at the second operation have had drainage of the common duct with palpatory or manual manipulation of the pancreas. For want of a better explanation we have interpreted this type of picture as due to some pancreatic toxin or ferment as the result of the surgical trauma with inadequate liver detoxification.

A second type of clinical picture occurs after a varying period of

time, usually the fifth day, in patients who have had a comparatively simple gall-bladder operation but who have been chronically jaundiced. A normal convalescence has been progressing up to the time of the onset of a slight degree of somnolence. They may or may not have lost large quantities of bile through external drainage. They slowly become stuporous and in the course of twelve to twenty-four hours pass into coma. The temperature rises to 103 or 104; kidney function has been adequate previously. There is no evidence of infection with the abdomen and the condition is not one of dehydration following too rapid loss of bile through the drainage tube. Nor has there been any increase in the obstructive cholangitis if this were present previous to operation. We have here a condition not unlike the coma of cholemia in a patient who is adequately drained and who has had no further increase of obstructive jaundice. We have fed these patients their own bile, either by allowing them to drink it or by giving it by stomach tube and have not prevented the fatal outcome by these procedures. This condition is essentially a coma, occurring in a patient with a diminishing obstructive jaundice. Are we dealing with a frank case of liver exhaustion similar to the terminal stages of a portal cirrhosis or an acute yellow atrophy of the liver?

Less frequently we have observed a third type of clinical picture that supervenes immediately after operations on the gall-bladder. This type is infrequent and it is interesting to note that it has occurred after rather simple types of operations on the biliary apparatus. This lethal complication has terminated, however, a long history of gall-bladder or biliary duct infection. These patients, as a rule, have not been jaundiced. The clinical onset is characterized by the onset of coma almost immediately following operation. The patient ordinarily does not recover from the anesthesia, a fact that should be noted. The temperature rises to 104 or 105, with marked acceleration of pulse, usually subsultus tendinum, carphology and talking delirium, and more rarely marked motor excitation. Chemical tests of the blood before operation demonstrated that kidney function was adequate and within normal limits. Spinal puncture after the onset of coma has revealed an increase in fluid under pressure, cell count of 10 to 15 per cubic mm., with two plus globulin reaction and negative Wassermann examination.

Whether the liver is primarily at fault in the three clinical conditions that I have outlined we do not know. The liver reacts to long continued or habitual toxic irritation by two pathologic processes, one the degeneration of liver cells and the other the proliferation of connective tissue. These processes apparently go on simultaneously, and as to which is secondary is of academic interest only. Certain it is that degenerating areas are replaced by connective tissue and in-

tracellular material, and that by replacement or contraction there is atrophy of liver parenchyma. It does seem reasonable, however, to assume that they are in some way associated with liver dysfunction. In their terminal manifestations they simulate in many ways the clinical conditions that are observed in diseases of the liver where there is a manifest loss of liver function. It is interesting to speculate whether there are not conditions of liver insufficiency which give a variety of minor symptoms, or that may exist without any symptoms for a long period of time by reason of the marked regenerative property of liver tissue. From the viewpoint of surgical prognosis may we not claim that these unrecognized cases of hepatitis are the cause of some of our unexplained mortalities and that contribute much to the morbidity that sometimes follows apparently the most successful type of surgical intervention? We believe that when an infection is once initiated within the abdomen and its course is chronic that the liver reacts in a variety of ways, but always with some degree of hepatic degeneration, and that in a certain proportion of cases surgical intervention in these cases is associated or followed by death due primarily to hepatic insufficiency.

PATHOLOGIC DISCUSSION (DR. MACNEAL)

The liver, as has long been known, is subject to acute purulent inflammations, secondary to severe purulent disease in the intestinal tract or in the gall-bladder and bile ducts. In the former instance the infectious agent evidently passes into the tributaries of the portal vein, frequently with evidence of thrombophlebitis, and reaches the branches of the portal vein in the liver substance, giving rise to multiple abscesses. When the primary disease is in the bile passages, on the other hand, the infection appears to ascend along the tributaries of the hepatic duct and the lymph channels accompanying these ducts, giving rise to multiple abscesses similarly distributed as in the first instance, but often containing brownish pus discolored by admixture of bile.

It is also well known that the liver is subject to very profound alteration of its structure as a result of slowly progressive inflammatory change, finally resulting in great diminution of the specific liver parenchyma and a more or less marked increase of the fibrous tissue of the capsule and the interlobular trabeculae. The etiology of these changes, which are designated by the general term, cirrhosis, is still somewhat obscure. In the atrophic cirrhosis of Laennec, the liver may become very small before death takes place. Here the injury is thought to be derived from the digestive tract, reaching the liver through the portal vein, and in some instances alcohol appears to have acted as the toxic agent. Contrasted with this is another well

defined type of cirrhosis, which follows upon chronic bile stasis and prolonged inflammation of the bile passages, known as biliary cirrhosis. Here there results an early interlobular and intralobular overgrowth of connective tissue, proceeding from the vicinity of the bile ducts. After a time such a liver also shrinks and becomes nodular, finally resembling the liver of atrophic cirrhosis.

It is also well established that the liver participates in a great variety of general diseases, especially the severe infections and intoxications.   In the acute stage of these one finds a round-celled infiltration of the interlobular connective tissue, degenerative changes in the liver columns, focal necrosis, or even massive necrosis of the liver substance.

Even in the absence of serious disease, the liver tends to become firmer with age, the interlobular and intralobular framework becoming gradually thickened while there is a relative or even absolute diminution of the parenchymatous elements with advancing years.

If the above statements be accepted as a hasty presentation of the better established conceptions in regard to liver inflammations, it will be evident that, in the present discussion, we are dealing with the more delicate shades of hepatic alteration, not those seen at autopsy in the body dead of severe infection, local or generalized, nor those of advanced atrophic cirrhosis, but rather those slighter alterations in the liver which have given rise to no clearly recognizable symptoms or signs, but may be regarded as accidental or incidental anatomic findings in patients whose abdomens have been opened on account of active or quiescent disease of variable degrees of severity, affecting other organs.   Under such circumstances an etiologic diagnosis of the liver condition is extremely hazardous and only the very bold may be expected to recognize with assurance in an individual instance a clear-cut relationship between the liver changes and the changes in other abdominal viscera.   Without additional evidence one should regard the observations only as suggestive of such a relationship.   In a field as obscure as this, however, even suggestive observations are of some value.

The liver alteration visible to the eye of the operator is usually an enlargement of the organ with rounding of its margins.   The enlargement is often general but frequently the right lobe or a portion of the right lobe near the gall-bladder may be disproportionately enlarged.   One may also see opaque bands of fibrosis in the liver substance near the gall-bladder.   This enlargement is evidently in part due to excess of fluid in the liver, congestion and edema, especially when there is an active inflammatory lesion in the gall-bladder or in the portal territory.   In many instances and especially when the enlargement is localized, it is evidently the result of growth of liver

substance. Apparently pressure of the body wall and of the internal organs influences to some extent the form of this overgrowth. In a minority of instances, the liver appears smaller and firmer than normal, suggesting an early atrophic cirrhosis. This condition may be regarded as a later stage of the process. Liver changes belonging in this category are so constantly observed in association with disease
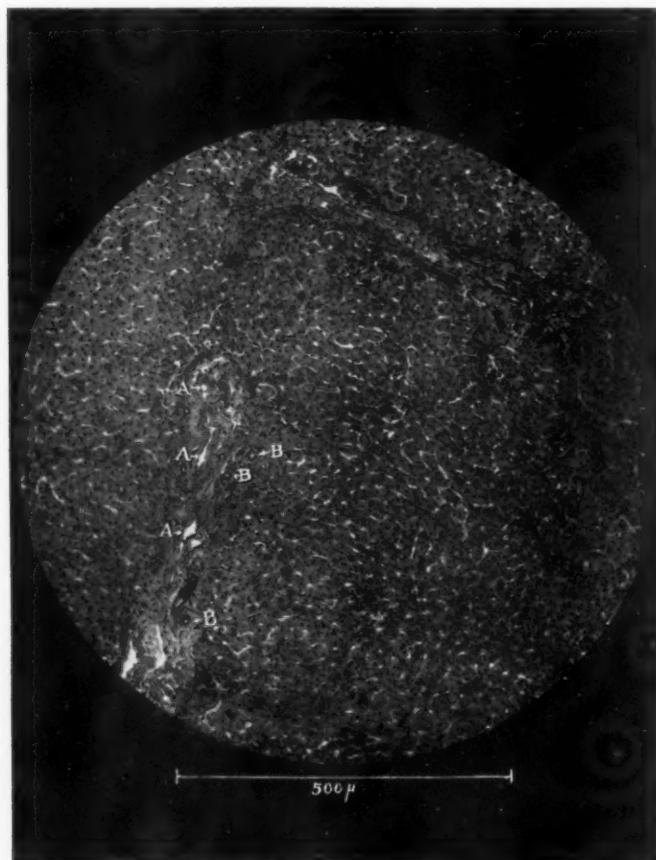
Fig. 1.—No. 25690, male, aged twenty-six: operative diagnosis, appendicitis, acute; operation, appendectomy. Gall-bladder negative. Liver presented diffuse white mottled appearance. Sections of liver showing moderate thickening of the fibrous trabeculae and infiltration with wandering cells, particularly near the bile ducts. Pathologic diagnosis, early stage of biliary cirrhosis. (A) Portal branches. (B) Bile ducts.

of the gall-bladder that a relationship between the two groups may be accepted as established.

Under the microscope one sees, in the soft swollen livers, a general dilatation of the vascular channels and a rich infiltration of the connective tissue trabeculae by lymphocytes and smaller numbers of polynuclear leucocytes. (Fig. 1.) In the more acute inflammations, the endothelial lining of the capillaries may be visibly thickened. In

the irregularly enlarged livers, the microscope reveals definite fibrous thickening of the connective tissue trabeculae and usually an excess of small bile ducts in this tissue. Lymphocytic infiltration of it is more or less marked, apparently depending upon the presence or absence of exacerbation of the inflammatory process. Liver lobules of irregular form and arrangement may be recognized and they doubtless indicate actual growth of liver substance. The firm smaller livers
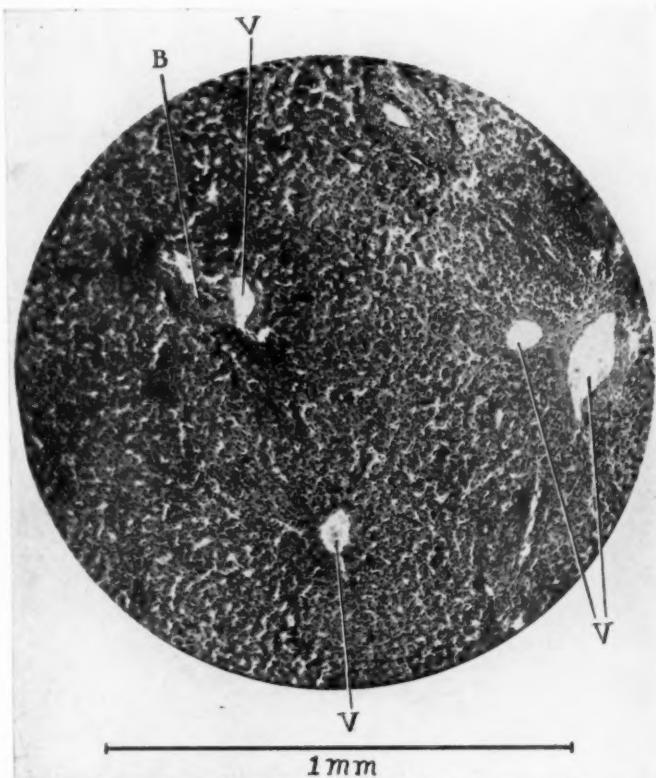
Fig. 2.—No. 25128, female, aged twenty-four: operative diagnosis, appendicitis, chronic; cecum mobile; operation, appendectomy, cecoplication. Gall-bladder negative except for more than normal vascularization. Sections of liver show considerable thickening with trabeculae of Glisson's capsule. Fibrous tissue is dense and hyaline, contains only a moderate excess of round cells. There is a moderate amount of brown pigment in the liver cells. The picture resembles the early stage of biliary cirrhosis but the hyaline character of the trabeculae shows that the process has existed for many months. Pathologic diagnosis; moderate biliary cirrhosis. *(B)* Bile ducts. *(V)* Portal branches.

reveal, under the microscope, a still more marked excess of fibrous tissue in the trabeculae. (Fig. 2.) Here the lobules may appear compressed with only narrow vascular channels. One may willingly agree that these three pictures represent stages of a single process, beginning with an acute phase of congestion, edema and exudation, going on to hyperplasia of liver tissue with repeated subsidence and recrudescence of the acute phase and eventually leading to marked over-

production of connective tissue, by contraction of which the paren-
chyma becomes irregularly compressed (Fig. 3). It should be noted,
however, that even when the appendix has shown evidence of prolonged
severe inflammation with adhesions all about it, or when the gall-
bladder has been the seat of similar long standing severe inflamma-
tion, the liver has not exhibited the very advanced diffuse alteration
characteristic of atrophic cirrhosis (Fig. 4). Indeed the liver appears
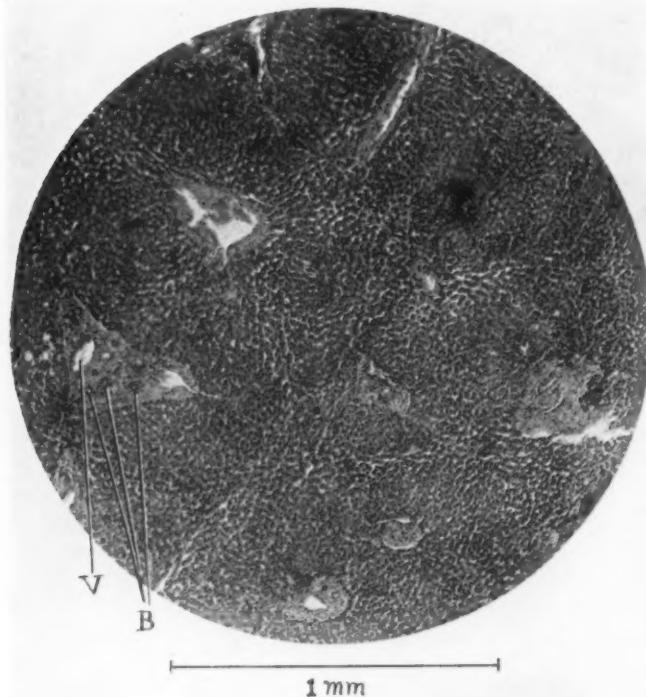
Fig. 3.—No. 24682, female, aged fifty: Operative diagnosis, cholecystitis, sub-
acute; cholelithiasis, appendicitis, chronic; operation, cholecystectomy, appendectomy.
Gall-bladder opaque, white walls, markedly thickened; contains 150 calculi sulphur
colored. Sections of the liver show marked thickening of the fibrous trabeculae
and occasional dense collections of round cells. Hyperplasia of bile ducts. Path-
ologic diagnosis, chronic interstitial hepatitis bearing some resemblance to that of
Laennec's cirrhosis. (B) Bile ducts. (V) Portal branches.

to withstand remarkably well the insults repeatedly coming to it
from these sources, so that one is impelled to look farther for the
explanation of the origin of more serious hepatic disease. The im-
portance of general disease, such as syphilis, tuberculosis and pro-
longed suppurations of distant parts as causes of liver pathology, is
not, therefore, eclipsed by the observations on hepatitis now under
consideration. It is, however, quite possible that chronic gall-bladder
suppuration might, of itself, induce a high grade of cirrhosis, but
certainly such an association appears to be relatively infrequent.

BIOCHEMICAL DISCUSSION (Dr. KILLIAN)

We have been fortunate in being able to study from a chemical point of view the last six cases of the third clinical group of Dr. Heyd. Of outstanding interest has been the observation that these patients

TABLE I

Threshold of alkalosis

Acidosis — Alkalosis

Acid ← 20 30 40 55 70 80 90 100 → Alkaline

CO_2 combining power
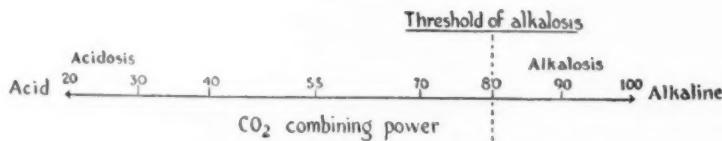
An increase in the carbon dioxide combining power toward 80 indicates an alkalosis; the reverse, an acidosis.


1 mm
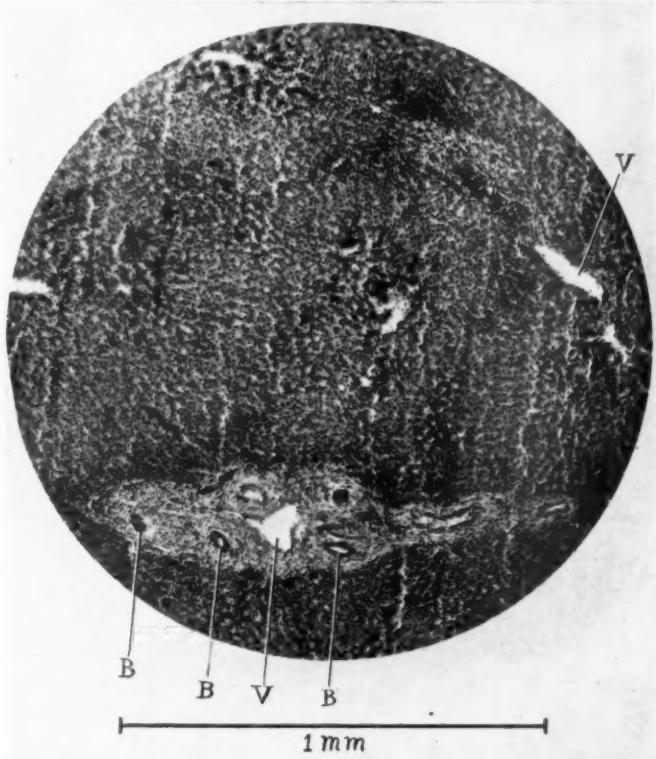
Fig. 4.—No. 26893, male, aged forty-six: operative diagnosis, cholecystitis, subacute; cholelithiasis, appendicitis, subacute; operation, cholecystectomy, appendectomy. Gall-bladder dirty brown color; about 400 fine sulphur colored calculi. Pancreas, abnormal hardness. Sections of gall-bladder muscle bundles irregularly thickened; in some places the muscle layer attains thickness of 1 mm. Sections of liver show very definite increase in fibrous tissue in the trabeculae of Glisson's capsule. The fibrous tissue is dense and evidently of considerable standing; contains an excess of round cells with very conspicuous bile ducts. Pathologic diagnosis, chronic interstitial hepatitis, evidently of biliary origin. *(B)* Bile ducts. *(V)* Portal branches.

show a carbon dioxide combining power markedly increased above the normal, representing 81 to 100 volumes per cent (Table I). This has not been due to the previous administration of alkalines and the

TABLE II

CHEMICAL BLOOD CHANGES IN DISEASES OF LIVER AND GALL-BLADDER

NO.	PATIENT	AGE	SEX	NON-PROTEIN N	UREA N	URIC ACID	SUGAR	DIASTATIC ACTIVITY	CHOLESTEROL	FIBRIN	CHLORIDES	CO_2 C.P.	REMARKS
				MG. PER 100 C.C.					PER CENT				
1.	M.D.	38	F.	54.7	10.1	4.2	0.093	20.4	0.146		0.53	47.1	Cholecystitis. No jaundice.
2.	N.M.	52	F.	46.0	22.1	4.1	0.227				0.428	98.0	Cholecystitis. 24 hours after operation. Na H CO₃ given by rectum.
												80.5	Na H CO₃ discontinued. HCL by mouth.
				38.5	19.1	3.6	0.093				0.350	49.0	One week later.
3.	M.K.	60	M.	45.0	16.3	3.7	0.150		0.290	0.357			Ca. of liver. Marked jaundice.
4.	L.Z.	57	F.	40.5	11.9	3.7	0.082	20.4	0.952	0.396	0.475	46.2	Cholecystitis.
5.	H.T.	28	F.	40.7	11.0								Marked jaundice. Obstruction of common bile duct.
				37.5	11.7	3.8	0.091	16.0	0.545	0.364			Two weeks after removal of obstruction. Three months later. Patient improved.
				44.1	12.3	3.7	0.098		0.182				Very slight jaundice.
6.	A.J.	42	F.	43.6	14.4	4.3			0.300			47.1	Cholecystitis and cholelithiasis. Jaundice.
7.	M.E.	41	F.	37.4	9.0	3.1	0.100	21.4	0.180	0.449			Cholecystitis. No jaundice.
8.	E.S.	50	F.	36.3	10.1	3.4	0.104		0.160				" " "
9.	V.S.	41	F.	32.7	7.5	4.1	0.084		0.154				" " "
10.	A.M.	43	M.	38.5	14.8	5.3	0.180	26.4	0.216			65.3	Cholecystitis and cholelithiasis.
11.	A.P.	37	F.	29.7	10.0	4.3	0.121	24.6	0.204			55.7	" " "
12.	B.M.	60	F.	21.9	8.9	2.4	0.148	14.8	0.313				Ca. of liver. Marked jaundice.

condition has been designated chemically as an alkalosis. So far as its fatal outcome is concerned it is much more pernicious than an acidosis. Of the six cases recently studied four terminated fatally and all of these were instances of chronic disease of the gall-bladder with simple operations. It has been determined that this increased carbon dioxide combining power is associated with a decreased hydrogen-ion concentration, and hence a true alkalosis exists.

For the observation of the chemical changes in the blood coincident with diseases of the liver and gall-bladder, seventeen cases have been studied, of which twelve are reported in the table (Table II). It will be seen that in many of these cases the nonprotein nitrogen exceeds the upper normal level of 30 mg. per 100 c.c. The urea nitrogen on the contrary does not show a corresponding increase, in fact, in some instances it is subnormal. These findings would indicate a corresponding increase in the rest nitrogen. Little is known concerning the nature of the compounds constituting the rest nitrogen of the blood, but we believe an intensive study of the nonprotein nitrogen partition of the blood will tell us more than we know at the present time concerning liver function. The normal uric acid content of the blood is from 3 to 4 mg. per 100 c.c. In a few instances an increase in the uric acid is noted. There are many reasons for attributing this increased uric acid to a mild secondary impairment of renal function. The normal blood sugar ranges from 0.09 to 0.120 per cent. In many cases of gall-bladder disease we find a mild hyperglycemia from 0.140 to 0.200 per cent. Associated with this increased blood sugar is an increased activity of the blood diastase. It is well known that the pancreas regulates the activity of this blood enzyme and an inhibition of pancreatic function entails an abnormal diastatic activity. Apparently, then, the increased blood sugar sometimes encountered in gall-bladder disease may find its cause in an associated disturbance of pancreatic function. On the other hand, in two cases we have found slight hypoglycemias. The reason for these hypoglycemias remains still a baffling question.

An increase in the cholesterol content of the blood has been observed in cases of obstruction in the biliary tract whether this obstruction is due to calculi, new growth or other mechanical means. The findings of Case 5 are of particular interest in this connection. At the time of entrance to the hospital this patient showed a blood cholesterol of 0.952 per cent and this was associated with a pronounced jaundice. At laparotomy it was found that during a previous operation for gall-bladder disease the common bile duct had been resected. The gall-bladder was drained by means of a rubber tube into the duodenum. Two weeks later the cholesterol had diminished to 0.545 per cent and

three months after operation had reached 0.182 per cent. At this time the patient showed but slight evidence of jaundice.

Since the liver has been regarded by some authorities as the site of formation of the fibrinogen of the blood, the fibrin content of the blood was studied in some cases. A few of these results are reported in the table. The normal fibrin content of the blood varies from 0.2 to 0.5 per cent. It will be seen that the figures fall well within the normal limits. These findings are of interest inasmuch as many of these cases manifested a delayed coagulation time. The calcium content of the blood sera of these patients was also determined. The calcium was found to be normal. This fact, however, does not contraindicate the use of dilute solutions of calcium chloride to decrease the coagulation time because for the process of clotting ionizable calcium is essential. When the total calcium of the blood serum has been determined there is no means of ascertaining the amount of this element that is ionizable. The chloride content of the blood was found to be normal except in those cases showing an increased CO_2 combining power. Here a decrease of the chloride concentration was noted.

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ACUTE PANCREATITIS*

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A CUTE surgical conditions of the pancreas may have two general divisions; those dependent upon factors peculiar to and inherent in the digestive functions of the pancreas and those definitely of an inflammatory nature. In the first group we have acute hemorrhagic pancreatitis, better designated as acute pancreatic necrosis. It is a condition not essentially inflammatory. The more severe cases end quickly in death or in recovery after massive gangrene, sloughing and suppuration. The milder cases recover promptly by a process of absorption and fibrosis. In the second group we have acute pancreatitis which is definitely inflammatory in character. It is comparable to the suppurative and nonsuppurative inflammations of the parotid gland.

It is the purpose of this paper to consider these two types of pancreatitis and to report cases of each.

CASE 1.—Mrs. M. S., a moderately heavy individual, age forty, began two weeks before the onset of her more serious trouble to have attacks of moderate pain in her upper abdomen. Three days before her death the patient suddenly developed a very severe epigastric pain with vomiting and continuous eructation of gas. The pain was more severe than the average gall-bladder colic and was not easily relieved by morphine. She had never had any previous attacks suggesting biliary disease but had been troubled with gas and pain after eating.

The patient was apparently in great distress. Her skin was cold, clammy, and cyanotic. The respirations were frequent but the lungs were clear. The temperature was 96; and pulse 150, scarcely palpable at the wrist. The abdomen was moderately tender in the whole epigastrium but more so on the right. There was only slight rigidity. No tumor was present in the upper abdomen but there was some distention. The white blood count was 33,000 and the polymorphonuclear cells 90 per cent. No sugar was present in the urine.

When the abdomen was opened under local anesthesia a large amount of coffee-colored or blood-tinged fluid escaped and many small areas of fat necrosis were visible in the omentum. The patient's general condition was so precarious that exploration was impossible. Drains were inserted and the abdomen closed. Death occurred in six hours and autopsy was refused.

Operation was ill-advised in this case. Every form of treatment will be found unsuccessful in the fulminating cases of pancreatic necrosis.

CASE 2.—Mrs. H. P. age twenty-three, quite fat and the mother of three children. During the summer of 1917 she had numerous attacks of upper abdominal pain. On Nov. 10, 1917, while at work, she was taken with very severe pain in the epigastrium and vomiting. The patient came under observation at the hospital on Nov. 12. Her temperature was 99.4, pulse 110. She was quite ill but

not in great shock. The abdomen was distended and tender but no tumor was palpable in the epigastrium. There was no jaundice and no sugar in the urine.

Within the abdomen was found a large amount of brownish red fluid, and in the omentum and over the peritoneum were many areas of fat necrosis. Below the pylorus, overlying the head of the pancreas, extending along the greater curvature of the stomach and even involving the transverse colon, was a large, hard, nodular mass with many clots and much gangrenous looking tissue. On palpation it felt not unlike a large carcinomatous mass. The lesser peritoneal cavity was opened with difficulty because of the extensive involvement. A finger was pushed into the mass in several places and into the region of the head of the pancreas. Large gauze and rubber tube drains were inserted to the mass and into the lesser peritoneal cavity. Many stones were removed from the gall-bladder and that organ drained.

The patient reacted well. The drainage from the region of the pancreas was enormous in amount, very purulent and very irritating. There was much slough-ing of fatty tissue. With the separation of the larger pieces there were fre-quent severe hemorrhages. The latter occurred at intervals for weeks and nearly cost the patient her life. One hemorrhage came on as late as the tenth week after operation and was so severe that the patient's pulse reached 160. The tem-perature ranged from 101 to 104, and the patient was very septic for weeks. Frequent bowel movements were troublesome for the first ten days after opera-tion but were due to a colitis and not to a pancreatic insufficiency. She showed no sugar in the urine at any time. The patient left the hospital after sixteen weeks with a pancreatic fistula which closed within a few months.

In 1923 the patient was seen with an acute cholecystitis. A stone was re-moved from the cystic duct and she has been entirely relieved. At this opera-tion the adhesions in the upper abdomen were so dense that little could be made out regarding the pancreas. At this time she had no sugar in the urine and the blood sugar was normal.

Of course it is perfectly evident that such a case as this could not recover without operation.

CASE 3.—Mrs. G. L., stout woman, age forty-three, and the mother of two children. Seventeen years ago, after the birth of a child, she had a severe at-tack of pain and soreness in her upper abdomen. Since that time, at intervals of a year or so, she has had a series of mild attacks of epigastric pain followed by a severe attack, usually with mild jaundice. For weeks before her admission to the hospital she had been having mild attacks with slight jaundice, vomiting, much gas, indefinite food distress, and a loss of twenty pounds in weight. Two weeks before coming to the hospital she had a severe attack. On careful ques-tioning she was unable to say that it was different or more severe than the four other serious attacks which she had experienced.

At the time of her operation she was entirely free from pain, but had a little soreness in the gall-bladder region. There was no palpable mass. The tempera-ture and pulse were normal.

On opening the abdomen the gall-bladder contained many stones and was con-siderably thickened. In the head of the pancreas was a hard, dark, nodular mass about three inches long. There was no free fluid in the peritoneal cavity. In the gastrohepatic omentum, just above the pylorus, was a large confluent area of fat necrosis. The gall-stones were removed and cholecystostomy done. Drains were placed to the pancreas and to the lesser peritoneal cavity. The mass in the pancreas was not disturbed.

This was considered to be a case of acute hemorrhagic pancreatitis which

had occurred two weeks before operation and from which the patient was recovering.

Following the operation no discharge came from the pancreas and the gall-bladder fistula closed in three weeks. She remained well for four months when she again had several mild attacks of pain followed by a very severe one. Two weeks after this her abdomen was again opened. There were no stones in the gall-bladder or common duct. There was no new area of pancreatic necrosis and the former area had undergone absorption and fibrosis. It was still palpable in the head of the pancreas but was much smaller and was firm and not nodular. There was no free peritoneal exudate and no evidence of fat necrosis, new or old.

The gall-bladder was removed as the probable direct or indirect cause of the trouble and she has remained entirely well. Since the removal of the gall-bladder and the exploration of the gall ducts this patient has had two attacks similar to her old trouble. They have consisted of several mild attacks of pain and soreness followed by a severe attack. There has been no jaundice. In other words, this patient has not been relieved by cholecystectomy.

Twice during her first admission she had a trace of sugar in her urine but there has been none since.

CASE 4.— Mrs. M. T., a rather slightly built woman, thirty-one years of age, the mother of two children. Two weeks before her present illness she had a severe attack of tonsillitis followed by soreness in her knees and ankles. Within a few days she was taken with a sudden, severe pain in the epigastrium, radiating to the back and with vomiting. Similar attacks continued for two weeks, occurring every two to three days and lasting several hours. There was moderate temperature, continuous soreness and the patient felt quite ill. She was admitted to the hospital after a severe attack lasting three days. Her temperature was 99.4, pulse 116, and the white blood count was 12,000. The whole upper abdomen was moderately tender. The skin was dry and slightly jaundiced. The urine contained no sugar. The symptoms and physical signs suggested acute cholecystitis but the diagnosis was uncertain. She was in much pain, looked ill, and was losing ground.

On opening the abdomen there was no free fluid. The gall-bladder was slightly thickened and edematous but contained no stones. About the common duct and in the retroperitoneal tissue around the head of the pancreas there was much edema. The pancreas itself was swollen to several times its normal size. It was not dark or nodular and there was no fat necrosis.

Cholecystostomy was done and drains were placed to the pancreas and to the lesser peritoneal cavity. The pancreatic tissue was not incised but the peritoneum about the head of the gland was opened with the hope of draining the edematous retroperitoneal lymph spaces. Bile drainage continued for three weeks but there was no purulent discharge from the pancreatic area.

The patient had no more attacks of pain and her general condition improved promptly. She has remained entirely well to the present time.

The etiology and pathology of acute pancreatitis is important because an understanding of it will be necessary before we shall be able to lay down the principles on which the condition may be intelligently treated.

In the inflammatory type of acute pancreatitis the infection reaches the pancreas most frequently along the lymphatic channels from a diseased gall bladder or from a peptic ulcer. It may also reach the pancreas as an ascending infection through the lumina of the bile

and pancreatic ducts. Less commonly it is carried by the blood from some distant focus or during a general systemic infection. Involvement by contiguity from an adjacent infection, usually a peptic ulcer, is possible.

The acute inflammatory type of pancreatitis is of less surgical interest than pancreatic necrosis because it is not often operable. The cases occurring in mumps and as catarrhal jaundice should not be operated. When operable the treatment of the inflammatory type of acute pancreatitis consists in prolonged drainage of the gall-bladder of common duct, removal of all sources of infection, as a diseased gall-bladder, an appendix, or a peptic ulcer. Pancreatic abscesses must be drained and an occasional pancreatic stone removed. It has been suggested that the pancreas be set at rest by giving an antidiabetic diet and by the administration of alkalies and also that pancreatic ferments be given to carry on pancreatic digestion.

Acute hemorrhagic pancreatitis is a sudden, massive necrosis of a considerable part of the pancreas. The area of necrosis is sharply separated from the uninvolved tissue and is accompanied by hemorrhage into the pancreas and surrounding lymph spaces. The peritoneal cavity, during the acute stage, contains a brownish or bloody exudate. In the fat about the pancreas, in the omentum and elsewhere, there are yellowish white areas of fat necrosis. These are due to the escape into the tissue of the fat splitting ferment of the pancreas. Fat necrosis indicates "some grave alteration of the pancreas," and is always present in acute hemorrhagic pancreatitis.

The real nature of pancreatic necrosis has not been determined. It has generally been considered to be due to the digestive action of the trypsin of the pancreas set free by some injury to that organ of a chemical or bacterial nature. The trypsin exists in the pancreas only as trypsinogen, a substance with no power to injure tissue. Within the duodenum, however, the trypsinogen is converted by the action of enterokinase into trypsin. The real problem then, on this theory, is to find what converts the trypsinogen into trypsin while still in the pancreas and how that agent reaches the pancreas.

Experimentally, acute pancreatic necrosis has been produced by injecting into the pancreatic tissue and into the pancreatic ducts certain irritating substances such as acids, alkalies, toxines, suspension of bacteria, artificial gastric juice, zinc chloride, ferments, bile salts, etc. On the other hand, the condition has been produced by the ligation of the pancreatic duct during active digestion and by direct trauma to the pancreas. It should be noted that in the pancreatitis produced by the ligation of the pancreatic duct and by trauma, bile, duodenal contents, and infection can play no part.

In man the only substances which can reach the pancreas by its

ducts are bile and duodenal contents. If bile is to enter the pancreatic
duct from the common bile duct, the two channels must join before
they enter the duodenum. We must also assume that something ob-
structs the diverticulum of Vater below their junction thus shunting
the bile into the pancreatic duct. Opie reports a case in which a
small stone in the diverticulum of Vater produced such an obstruction
and Archibald suggests that it is due to a spasm of the sphincter
at the diverticulum of Vater. He also suggests that the spasm may be
due to some irritation such as an ulcer or hyperacidity.

Flexner has shown that bile, rich in bile salts, especially tauro-
cholate, is more irritating to the pancreas than normal bile. He has
also demonstrated that mucin in bile tends to lessen its irritation. It
has also been proved that infected bile will cause pancreatitis when
normal bile will not.

Given then an obstruction at the diverticulum of Vater, a concen-
trated, infected bile, poor in mucin, and an increased pressure within
the ducts and we have the stage set for an attack of acute hemorrhagic
pancreatitis according to the bile theory.

This theory undoubtedly does explain some cases of pancreatic
necrosis but not all of them. It cannot explain cases when the com-
mon bile duct and the pancreatic duct enter the duodenum separately;
and even if they do join in the diverticulum of Vater it is probably
rare for the anatomic condition to be such that a small stone or a
spasm of the sphincter can convert them into a continuous channel.
Granting proper anatomic arrangements and it is still doubtful, ac-
cording to recent experiments, whether sufficient pressure is exerted
in the duct of Wirsung to drive normal bile into the pancreas with
enough force to cause pancreatic necrosis. However, while proper
anatomic and physical conditions may be rare, yet the cases of pan-
creatic necrosis are equally rare and we have in addition to the action
of normal bile that of the more irritating concentrated bile and of the
infection it carries.

Closely allied to the bile theory of pancreatitis is the theory that the
injection of duodenal contents into the pancreatic ducts might be
responsible for the condition. It contains ferments capable of con-
verting trypsinogen into trypsin and experimentally when injected
into the pancreatic ducts it will cause pancreatic necrosis. Against
this theory is the fact that it has been impossible to drive fluids from
the duodenum either into the duct of Wirsung or Santorini. However
it has been suggested that when the common bile duct and the duct
of Wirsung unite in the diverticulum of Vater, a gall-stone passing into
the intestine might so paralyze the sphincter as to allow a reflux of
duodenal contents from the duodenum. In certain cases of acute pan-

creatic necrosis gallstones are known to have recently passed into the duodenum.

Another theory of the etiology of pancreatic necrosis and one which fits in well with the clinical circumstances is that the activating agent is an infection entering the pancreas through the lymphatic channels, most commonly through those from the gall-bladder or liver but also through those from the appendix, stomach, or duodenum. The infection is supposed to cause enough injury to the pancreatic tissue to set free a substance capable of activating the trypsinogen and thus starting the process of destruction. In this connection it should be noted that leucocytes and bacteria within the pancreas may produce a ferment with the power of activating the pancreatic secretion. The original inflammation is relatively so small as to be entirely lost in the massive process which follows.

Against this theory is the fact that the pancreatitis is not always associated with a demonstrable infection in the gall-bladder or elsewhere and that the passage of an infection from the gall-bladder and other organs through the lymph vessels to the pancreas involves the supposition of a retrograde flow in the lymphatic channels. If we admit the possibility of lymph-borne infection activating the pancreatic secretion we must also admit the possibility of a blood-borne infection doing the same thing. Experimentally of course it has been impossible to produce pancreatic necrosis by infection through the pancreatic lymphatics.

Gallstones and infections of the gall-bladder and gall ducts have been found in a very large percentage of the cases of acute pancreatitis and it seems highly probable that they are an important factor in the etiology. Whether it is due to the bile entering the pancreas or to the infection reaching the pancreas by the lymphatic vessels remains to be decided.

The profound shock and the early deaths occurring in acute hemorrhagic pancreatitis are probably due to the absorption of autolyzed pancreatic tissue. Experimentally when such tissue has been injected into the peritoneal cavity of a dog, shock, early death, and other symptoms, as in acute pancreatic necrosis, have occurred. Of course we must not lose sight of the fact that we have a massive and sudden destruction of tissue in the immediate neighborhood of the large sympathetic ganglia.

The diagnosis of acute pancreatic necrosis is difficult and is usually made at operation or autopsy. It is most often mistaken for acute trouble in the gall-bladder or ducts or for an acute perforation of the stomach or duodenum, occasionally for acute appendicitis or acute ileus.

It is well to remember that there are severe cases and relatively

mild ones. The severe cases with their extreme pain, profound shock, subnormal temperature, cyanosis, coma, and early death have been generally assumed to be typical of acute hemorrhagic pancreatitis and the fact that there are mild cases which cannot easily be distinguished from attacks of cholecystitis, has not been sufficiently emphasized.

There are no pathognomonic signs or symptoms of acute pancreatic necrosis. The cases are often difficult because they frequently occur in patients who have had recurrent trouble in the gall-bladder or stomach and in patients too ill to give definite information.

The pain of pancreatic necrosis comes on rather suddenly and is overwhelming in character. It is continuous but varies in intensity. It is not easily relieved by morphine and the patient seems to be in great distress. It is located in the epigastrium but is often felt across the back. The tenderness and rigidity when seen reasonably early are not so marked or extensive as in perforating ulcer. They are mostly above the navel and extend to the left of the mid-line. The extension of the epigastric tenderness over the mid-line to the left side is an important sign and carefully observed may lead to a diagnosis of pancreatitis. Of course if the case is seen late when peritonitis has developed it will be useless as a specific sign of pancreatitis. When the tail of the pancreas is involved there may be tenderness in the left costovertebral angle. The abdominal respiratory movements are not entirely abolished but deep breathing is impossible. The vomiting is a very constant symptom and is very persistent and frequently associated with much eructation of gas. It is never fecal until general peritonitis has developed. The abdomen is usually flat with some distention above the navel. There is not often a clear cut tumor mass but rather an indefinite transverse resistance in the upper abdomen due to the enlarged, deep-seated pancreas. Early in this condition the temperature is subnormal but later with the beginning peritonitis it is increased. The pulse is weak and the patient shows many more signs of shock and collapse than in perforating ulcer or acute gall-bladder disease. The dull, leaden paleness and sunken features of shock combined with cyanosis give a peculiar appearance. Movable dullness can sometimes be made out in the abdomen although the amount of fluid is usually not sufficient for this. It may be useful to remember that in early perforations of the stomach or duodenum some gas usually escapes into the peritoneal cavity and can with certainty be made out by x-ray. Its presence might easily differentiate between acute pancreatitis and perforating ulcer.

In these very acute conditions of the pancreas sugar in the urine, diarrhea, and the various laboratory tests of pancreatic insufficiency are not of much value from a diagnostic point of view.

The treatment of acute hemorrhagic pancreatitis is surgical. Mild

cases however often recover without operation. The custom of not operating upon cases of acute cholecystitis is undoubtedly responsible for the failure to discover many moderate cases of acute pancreatitis. The object of surgical intervention is to provide drainage for the toxic products of pancreatic degeneration; to avoid the immediate extension of the necrosis and to prevent future attacks.

How much we can accomplish in checking the rapid intoxication in acute hemorrhagic pancreatitis by drainage to the pancreas during the early stages of this disease, we do not know. It has been stated and supported by good experimental work that the bloody peritoneal exudate found at operation is harmless. Incision or blunt punctures into the necrotic pancreas are of doubtful value or expediency. All collections of encysted fluid in and about the pancreas should certainly be evacuated. This will include drainage of the lesser peritoneal cavity. As absorption of toxic material is largely through the retroperitoneal lymph spaces, drainage should be established by incisions through the peritoneum about the necrotic pancreas when local conditions permit. Drainage, of course, is used not only to prevent the immediate absorption of toxic substances but to give exit later to the massive products of gangrene and suppuration which usually develop in the extensive cases of pancreatic necrosis. Whether it is possible by operation to prevent the further extension of this pathologic process we do not know. It is probable that the extent of the necrosis is determined in the first few minutes of the trouble and that no further tendency to extension exists. However, if injection of bile under pressure from the common bile duct into the pancreatic duct is the etiologic factor in pancreatic necrosis, drainage of the gallbladder or common duct will remove this pressure and prevent the further extension of the pathologic process. Archibald has suggested that the pressure in the common duct may also be relieved by cutting the sphincter which closes the diverticulum of Vater as it is his theory that a spasm of this muscle is an essential factor in the increase of pressure in the ducts.

The prevention of future attacks of acute hemorrhagic pancreatitis consists chiefly in the elimination of infections from the gall-bladder and ducts of the liver, as well as that from a peptic ulcer or a diseased appendix. Whether we believe that the disease is due to injection of bile into the pancreas or results from infection carried to the pancreas through the lymph channels, the infection is an all important factor.

The actual operation for acute hemorrhagic pancreatitis will consist in evacuation of the peritoneal exudate, drainage of the area of pancreatic necrosis and of the lesser peritoneal cavity, incision into any collection of fluid in or about the pancreas and drainage of the

gall-bladder if the patient's condition will permit. Removal of stones from the common duct and excision of the gall-bladder will rarely be justified in acute pancreatitis. However, cholecystectomy is much more certain to prevent further attacks of pancreatitis than cholecystostomy. Drainage of the gall ducts should be prolonged for several weeks if possible. Permanent drainage of the gall-bladder into the stomach or duodenum by cholecystogastrostomy or cholecystenterostomy is not a good procedure for acute pancreatitis. Archibald's operation of cutting the sphincter at the diverticulum of Vater through an opening in the duodenum has not been generally accepted by the profession.

SUMMARY

(1) Acute surgical conditions of the pancreas include the noninflammatory pancreatic necrosis and true inflammatory pancreatitis.

(2) Acute pancreatic necrosis is probably due to activated pancreatic ferments escaping into the pancreas and surrounding tissue.

(3) The activating agents may be bile, duodenal contents, or infection.

(4) The frequency of gall-stones, and infections of the gall-bladder and ducts is certainly significant.

(5) The cause of the profound shock is absorption of autolyzed pancreatic tissue.

(6) The most helpful diagnostic points are the severity of the pain, the collapse, and the extension of the epigastric tenderness to the left.

(7) The object of surgical intervention is to remove dangerous toxic substances, prevent the extension of the pathologic process, and avoid future attacks.

227 MICHIGAN STREET.

CARCINOMA OF THE CERVIX ASSOCIATED WITH PREGNANCY*

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THAT "educating the public" on the cancer question has not been universally accomplished will be evident from a review of the following history.

About March 1, 1922, Mrs. P. M., a farmer's wife, thirty-two years of age, began to notice a grayish white, watery, vaginal discharge, at times slightly streaked with blood. A little later she experienced some vesical irritation and the discharge became more profuse and distinctly offensive. At irregular intervals the flow of bright red blood almost amounted to a hemorrhage. From March 1 to about June 1, 1922, it was practically constant. After this date, presumably after pregnancy had supervened, there were more or less extended intervals between the bleedings. At one time there was no sign of blood for three weeks. She had backache and pain in the lower abdomen. The pain was intermittent and lancinating in character and it radiated into both hips and thighs. At rare intervals, it was momentarily quite acute. These symptoms continued for ten months. She then contracted a severe cold. The frequent, paroxysmal cough incident to this illness resulted in such violent hemorrhage from the vagina that the family physician was finally called. She confided to him the information that she considered herself about four and a half months pregnant and that she was having a miscarriage. She declared that she had "felt life" several days before. Her doctor, P. H. Hastings of Alta Vista, Iowa, did not find the situation so simple and on January 18, 1923, he kindly afforded me an opportunity to see her.

She was a small gracile blonde of Norwegian parentage. She did not appear to be especially anemic and was fairly well nourished. She complained of weakness, loss of appetite, nausea and pain in the lower abdomen. Her mother had "liver trouble" and died of intestinal obstruction. When quite old her father died of pulmonary tuberculosis. One sister died of "heart trouble" and a brother died of typhoid. She has five brothers and three sisters living and well.

She began to menstruate regularly every twenty-eight days when she was eleven years old. She never experienced any discomfort or pain during her periods.

She married when she was seventeen years of age and bore eight healthy children. Her labors were remarkably easy. She stated that no doctor had ever attended her because none had ever been able to arrive in time.

In 1920 she had influenza for two weeks. She did not make a good recovery from this illness and never fully regained her former strength and endurance. She mentioned this circumstance as an excuse for having disregarded symptoms so striking and significant, which she began to exhibit nearly a year before calling a physician for her present illness.

Inspection and palpation of the enlarged abdomen at once confirmed the diagnosis of a rather advanced pregnancy. There was a profuse and very offensive bloody discharge from the vagina. On bimanual examination the larger part of the vagina was found to be occupied by a cauliflower shaped tumor arising from the anterior

lip of the cervix. It was friable in consistency and when touched it bled freely.
I might say that the vaginal examination was unusually difficult, not only on
account of the very high position of the cervix and the presence of the large vascular
tumor, but more especially because the perineum was intact and quite unyielding.
Such integrity of structure and function will appear truly marvelous when we
bear in mind that this little woman had in relatively rapid succession eight pre-
cipitate labors.

On January 27, 1923, the patient was brought to St. Joseph's Hospital, New
Hampton, Iowa. Here she was again carefully examined and so far as we could
determine the growth was really local in extent. The mucosa of the vagina was
not involved, enlarged glands could not be palpated and the cervix was still movable.
The blood pressure was normal and only a trace of albumin was found in the
urine. The white cell count was 8,000 and hemoglobin was 75 per cent.

A good share of the responsibility for the immediate management of the condition
was assumed by the patient herself and her family. No active intervention could
be considered until after the child was viable.

Under the direction of Drs. Wm. L. Brown and Lester R. Parson of Chicago,
and Prof. John G. Clark of Philadelphia, 100 mg. of radium were applied to the
growth for twenty-four hours. A considerable constitutional reaction followed in
due time. However, at the end of about fifteen days the patient's general condition
was very satisfactory. The fetus was alive and apparently thriving. The local
effect of the radium certainly constituted a striking therapeutic result. A mere
remnant was all that remained of the tumor at the end of four weeks.

On March, 27, 1923, severe labor pains began. In spite of two quarter-grain
doses of morphine the patient suffered much. At the end of eighteen hours the
long, thick-walled cervix barely admitted one finger.

An abdominal cesarean section was done and a live female child delivered. After
the removal of the placenta a panhysterectomy was performed. At the conclusion
of the operation the patient seemed to be in very fair condition. But soon after
having been brought to her bed she suddenly collapsed and died in a few minutes.
About three hours later the child also expired.

A result so tragical in its consequences to this young family may
well serve as a text for a few clinical reflections.

In the first place it seems almost incredible that symptoms so char-
acteristic of cancer of the cervix could be entirely disregarded for
ten months. Moreover, after the most critical interpretation of these
symptoms there can remain no doubt that the pregnancy supervened
months after the carcinoma was well established.

We may conclude too that results in the treatment of this class of
cases will not improve until there is more prompt and intelligent co-
operation between patient, family physician and obstetric specialist.

While it is true that our patient ascribed her general loss of strength
to the attack of influenza in 1920, the clinical manifestations of cer-
vical cancer were singularly striking and definite in their onset. "The
first week in March" was repeatedly and invariably mentioned as the
date when the pain in the lower abdomen, the leucorrhea and the
irregular hemorrhages from the vagina were first noticed.

Thaler of the Peham Klinik has lately cited figures to show that
carcinoma of the cervix is more apt to occur in women who have ex-

hibited a deficient ovarian function as manifested by late appearance of the menses, irregular amenorrhea and an early menopause. Our patient certainly did not conform to this type. It will be remembered that she began to menstruate at eleven and that within fourteen years she had nine children. This tendency of carcinoma of the cervix and pregnancy to coexist in multipara who have had many pregnancies in rapid succession has often been observed. In 1909 John T. Williams wrote that "In the entire literature I have been able to find only eight cases of this clinical combination in primigravida. In the histories of 43 cases I have found the average number of pregnancies to be 6.9, a proportion, of course, much above the average."

Many authors have published their observations on the subject of carcinoma and pregnancy. And a more bewildering and contradictory expression of opinion, on every possible phase of the question, can hardly be imagined. I suppose that this "confusion of ideas" depends on the fact that pregnancy and carcinoma are in themselves contradictory terms. At any rate, the influence of age will render the coexistence of these two conditions comparatively rare. In the busy practice of a life time a physician might be fortunate enough never to see this combination. That the discovery of such a rare clinical situation may depend on mere coincidence is well illustrated by an account published in 1909 by Gräfenberg from the Pfannenstiel Klinik at Kiel. Within a few weeks three cases of pregnancy associated with carcinoma of the cervix were observed and operated, while for many years this complication had not been seen in this Klinik. So at the Chicago Lying-in Hospital and Dispensary, among 24,200 consecutive obstetric cases there was only one complicated by cancer of the cervix. Just lately E. O. Gross has reviewed 224,080 obstetric cases. One in every 1538 was complicated by cervical cancer. Moreover, this observer contends that the complication of carcinoma in pregnancy and labor is five times more frequent than is ordinarily believed. According to his calculation the exact status of this question can be determined only when the cases are observed for a year postpartum. Of 34 cases studied in this way there were 24, or 66.7 per cent, in whom the carcinoma coexisted with the pregnancy. So that the possibility of cancer of the cervix should be borne in mind, not only for a year after a full term gestation and puerperium, but that the same rule should be applied after every interruption of pregnancy. But even on this point opinions are by no means unanimous. Just a few months ago Schweitzer again emphasized the importance of trauma incident to delivery as an etiologic factor in carcinoma of the cervix, while Mason and Konrad have called attention to a "tem-

porary retardation of its growth coincident with involution of the uterus.''

Authorities do not even agree on the simple question whether the carcinoma antedates the pregnancy, or whether it generally develops after the pregnancy has become established. Cohnstein found that the malignant process preceded the gravid state in only 17 per cent of his 127 cases. These figures agree practically with those published by Gross only last year. In five or 16.7 per cent of the 34 cases reported it was demonstrated clinically that the carcinoma existed before the pregnancy. It is significant too that in every one of these five cases spontaneous abortion occurred. However, most clinicians agree with John T. Williams, John W. Williams, Blumreich, Keyes, Sarvey and Schweitzer that ''in the majority of instances the woman already has a carcinoma and then becomes pregnant.'' This was undoubtedly the sequence of events in our patient.

The influence of pregnancy on the clinical behavior of cancer of the cervix is a subject still under discussion.

It is true, though, that most observers express the view that ''carcinoma of the cervix as a rule, grows with great rapidity during pregnancy.'' In this connection the classical experiment of Zweifel is often mentioned. ''He marked by means of a loop of thread the border line between the healthy and the diseased parts in a case of cancer during pregnancy. A fortnight later the disease had progressed about two fingers' breadths, no doubt a proof of the enormous growing tendency in this case.'' The case of Simpson is often quoted. ''In three months he saw a carcinoma invade cervix, bladder and rectum.''

This sweeping statement certainly ignores a considerable and astute minority opinion. Spiegelberg, Noble, Pinard, Varnier, Herbert Spencer, Penris, v. Siebold, v. Graf, Oskar Frankl and A. Meyer are among the authorities who ''consider the rapid growth of carcinoma during pregnancy by no means proven.''

In view of these conflicting opinions one is fairly driven to the conclusion that there is a comparatively benign and a more malignant type of carcinoma. And it may be assumed that encouraging statistics in a small series of cases depend largely on this circumstance. At any rate, so long as the real nature and the specific cause of cancer remain unknown all arbitrary assertions in regard to its clinical behavior and treatment are obviously ''out of order.''

On the one hand we are told that hyperemia, vascular and lymphatic hypertrophy of connective tissue incident to pregnancy accelerate the growth and aggravate the symptoms of carcinoma. On the other hand, it is contended that these conditions resist the invasion of malignant disease. It is pointed out that carcinoma thrives in old,

anemic, biologically decrepit, arteriosclerotic, poorly nourished scar tissue, tissue deteriorated by chronic inflammatory processes.

E. O. Gross suggests the inquiry whether the few contradictory but nevertheless authoritative observers whose conclusions may be accepted without doubt, cannot be explained on the different histologic structure of the carcinoma. According to this explanation the medullary type of growth would be considered the rule while the scirrhus form would be regarded as the exception. Years ago Oui had in mind, no doubt, the same thought when he said that the evolution of carcinoma of the cervix, one could almost say of all cancers, is so variable that it is impossible to affirm, in a given instance, that the evolution was accelerated by the pregnancy. The same view was again emphasized by Friederich Wolf only last year. He states that "in our researches on the efficiency of operative and ray treatment of carcinoma in general," and this may be applied as well to the combination of carcinoma and pregnancy, "it is often observed that there are relatively benign carcinomas and that there are atypical, rapidly growing tumors." As usual C. H. Mayo has some pertinent observations to make on this problem. He has found that "the possibility or rather probability of the cure of cancer can be largely foretold by the pathologist: thus two individuals of the same age with cancer of the breast, stomach or rectum of the same period of growth with the same extent of apparent glandular invasion would have prospects of life following the same operation, very largely according to the presence of fibrosis in the one and its absence in the other."

Bearing in mind the anemia, the loss of strength, the endometritis, the extension of the disease to the mucous membrane of the body of the uterus, the infiltration of the lower uterine segment, the chemical changes in the secretions and the distortion and obstruction of the cervical canal, one would suppose that conception would be prevented, or, at any rate, that if pregnancy did supervene it would be interrupted at an early date. Age, social state, the extent of involvement of the tissues, the type of tumor are all factors which tend to determine the influence of the carcinoma on the probability and on the course of gestation. According to W. Roger Williams, "when the disease is limited to the cervix, gestation relatively often goes on to full term."

Naturally, the prognosis so far as the child is concerned will depend very much on the character of the treatment instituted. A hysterectomy performed immediately after the diagnosis of carcinoma has been made will result, of course, in a high fetal mortality. If the condition is inoperable, and if the child is delivered at or near term its prospects for life are of course relatively good. But Edgar makes the observation that after "cancerous cachexia stillbirths are very

common, while children born alive are very weakly and, in many cases, succumb soon after birth. The toxins which must be present in the maternal blood appear to exert an influence on the fetus which is similar to that observed in tuberculosis.'' This description tallies accurately with the condition of the child in our case.

At the present time there are few clinicians who would agree with the famous dictum enunciated by Bouilly and approved by Pinard, Varnier, Commandeur and Champetier de Ribes. According to this postulate, ''whatever the management may be, a pregnant woman who has a cancer of the uterus is lost.'' It is obvious that such an attitude would improve the prognosis so far as the child is concerned in many instances.

In a woman who has cancer of the uterus labor is usually a dramatic affair. There is hardly a disaster known to the science of obstetrics that may not happen in this situation. Slow dilatation, uterine inertia, a tedious, painful labor resulting in general exhaustion, laceration of the cervix, extending deep into the parametrium, the bladder and all degrees of hemorrhage, rupture of the uterus, peritonitis, sepsis, missed labor, and absolute obstruction to delivery are all complications that the obstetrician may need to recognize and to treat.

And it should be realized, at once, that these calamities may ensue not only in the course of the more advanced conditions but that they may follow even a slight carcinomatous infiltration of the cervix.

It is often assumed that the pressure and friction of the fetus on the growth during labor causes a dissemination of carcinoma cells resulting in the more rapid growth of the tumor.

It is generally believed that, other things being equal, spontaneous labor is more apt to occur when the posterior lip is primarily involved than when the neoplasm has issued from the anterior lip. The diagnosis of uterine cancer is easy, as a rule. It needs to be differentiated from incomplete abortion, hydatiform mole, concealed retroplacental hemorrhage, benign polypi and fibroids, inflammatory masses, cervical erosions and placenta previa. On three occasions DeLee found ''a hard, nodular but not ulcerative condition of the cervix during the middle of pregnancy attended by slight bleedings and fetid discharge, but which were not carcinomatous and which disappeared after delivery.''

In a thorough study of the literature I have not found any evidence which would even tend to show that excision of a specimen from the cervix, if done in approved modern fashion, results in any deleterious consequences either to mother or child. Accordingly, before a diagnosis is ventured, every bleeding multiparous woman should be examined with a speculum and if any questionable tissue is found it should be examined by a competent pathologist. And in this con-

nection it is well to bear in mind the old observation that a given pathologic lesion does not always result in a corresponding clinical exhibition of symptoms. So, in a given instance the classical manifestations of carcinoma of the cervix may not appear until it is far advanced. Schweitzer has lately reported two such cases. Although operated rather late, in neither one had there been any hemorrhage.

The same author has observed a sort of parallelism between the stage of pregnancy and the extent of the carcinomatous process. In other words, a carcinoma seen during the second month of pregnancy was found to be just beginning, patients examined about the middle of pregnancy showed more advanced but still local lesions, while in those women who came to examination after the seventh month the carcinoma involved the vagina, the pelvic glands and in one instance the entire cervix.

The early diagnosis of pregnancy associated with carcinoma of the cervix is even more difficult than it is under normal conditions. Hemorrhages due to the carcinoma may, of course, simulate the menstrual flow and on this account the actual cessation of the menses may not be recognized.

Moreover, it is only human that the possibility of a combination so rare may never occur to the clinician. About the only point on which all authorities agree is that the prognosis is extremely grave. ''Any kind of treatment may result in the death of both patients'' is about the unanimous verdict on this question.

In our case, one of the outstanding clinical features was the fact that after typical symptoms had continued for about a year the condition was still operable. And I might say that the operation was comparatively easy. The test of operability is hard to define. It is generally agreed, however, that when the broad ligaments and pelvic glands are not involved and when the cervix is still movable, hysterectomy is feasible.

But even more problematical than the question of operability is the problem of deciding in a given instance whether labor will deliver the child spontaneously.

Influenced by the striking though temporary result of radiation and by reports of safe deliveries even in inoperable cases we decided to give our patient a test of labor. That this decision contributed to the unfortunate fate of our patients it would be foolish to deny.

In the light of this experience I venture to submit the suggestion that a pregnant woman who has a cancer of the cervix which has been subjected to radiation should not be permitted to go into labor. The hard cicatricial cervical tissue will not yield. At the end of some hours we will have added to our original difficulties an exhausted patient and a mutinous environment.

In a review published a short time ago Cathala and Mérat found only eight cases of cancer of the cervix complicated by pregnancy which had been treated by the application of radium. To these eight cases they add one they observed and treated. Naturally, they do not attempt to formulate any positive conclusions from so limited a number of observations.

But they have thoroughly succeeded in submitting a number of interesting questions. "What are the indications in the face of cancer of the cervix who is six months pregnant? It is clear that at this stage of development the child should be permitted to grow. Is it not possible by applications of radium to cure the neoplasm, or at least to retard its growth? In the majority of instances the child has survived the radiations. But if the radium does not kill the fetus is it not to be feared that it will determine lesions of the brain cells which will compromise the intellectual future of the child? Can one hope to cure the mother, and at the same time spare the life of the child during the early months of gestation? In that case should the radium be applied in large or small frequently repeated doses?" They conclude their interesting contribution by the general statement that the problems presented require for their solution further study and experience.

In addition to the nine cases reviewed by Cathala and Mérat, Gross has reported two operable cases who were subjected to intensive radium treatment. In both patients criminal abortion interrupted the pregnancies. In both instances, rapidly progressive, inoperable local recurrence closed the clinical drama. Field treated a case of carcinoma of the cervix associated with pregnancy with immense doses of radium. The woman died within a year from the effects of metastatic carcinoma of the liver.

Weibel advises against every kind of actinotherapy on account of its destructive influence on the child. Bottaro and de Bengoa have coined the new word "Rochar" from the initials of the procedures to be successively employed in the treatment of carcinoma of the cervix in pregnancy. Radium, observation, cesarean, hysterectomy, adnexectomy and radiation is the sequence of measures thus graphically recommended.

It is hardly worth while to consider at any length the merits of the various refinements of technic suggested from time to time for the execution of the several radical operations. They differ in no essential particulars from those employed in nonpregnant patients.

It is, of course, strictly in accordance with modern tendencies to avoid shock and hemorrhage by every feasible means. Mason and Konrad have suggested that this may be accomplished by paravertebral anesthesia and a two-stage operation. "The panhysterectomy

whether by the abdominal or vaginal route'' is postponed until the patient shall have recovered from the shock of the primary cesarean section.

But an early recognition of the tumor is the factor which determines the clinical fate of a pregnant woman who has a cancer of the cervix.

It has already been emphasized that these tumors exhibit various degrees of malignancy. And it is safe to say that a majority of the cured cases have been of the squamous-cell type. This was the diagnosis in our case made by Prof. Ed. L. Miloslavich of Milwaukee. It is my impression that in this instance the pregnancy did not materially influence the growth of the tumor. That it did not accelerate its extension is conclusively evident from the fact that it was readily operable after the symptoms had continued for over a year.

CONCLUSIONS

1. A considerable proportion of the public is still in need of instruction on the cancer question.

2. Carcinoma of the cervix associated with pregnancy is a rare combination.

3. Trauma incident to labor or abortion is an important etiologic factor.

4. Women who have borne many children in rapid succession are most likely to develop this condition.

5. Accordingly, for a year subsequent to pregnancy multipara should be watched with especial care for the early evidences of malignancy.

6. So long as it remains local, carcinoma of the cervix does not cause sterility.

7. In rare instances carcinoma of the cervix may coexist with pregnancy for an extended period without exhibiting any clinical manifestations.

8. As a rule there exists a certain ''parallelism'' between the stage of pregnancy and the degree of advancement of the malignant growth.

9. In the majority of cases the carcinoma antedates the pregnancy. But it is not always an easy matter to determine this question.

10. That there is a comparatively benign and a more malignant type of carcinoma has often been observed. And it is more than likely that statistics of extraordinary results, in a small series of cases, depend largely on this circumstance.

11. The results of animal experimentation with cancer cannot be applied, without modification, to human individuals.

12. It has not been proved that the incidence of pregnancy invariably causes the tumor to grow with increased rapidity.

13. Excision of a piece of the cervix will injure neither mother nor fetus.

14. Carcinoma of the cervix complicated by pregnancy must be differentiated from placenta previa, varicose veins, accidental hemorrhage, and benign tumors.

15. "Therapeutic abortion is strictly contraindicated in these cases." (Edgar.)

16. Just how much consideration is to be given the unborn child will depend on the ethical sensibilities of the patient and her physician.

THE CLINICAL SIGNIFICANCE OF CHEMICAL AND SERUM ANALYSES OF THE BLOOD OF UTERINE CANCER CARRIERS SUBJECTED TO MEASURED RADIATION DOSES*

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ROENTGEN and radium ray sickness has interested clinicians for some time. Walsh,[1] in 1897, was probably the first to recognize and describe this reaction. Pfahler[2] attributed the symptoms to poor ventilation of the roentgen ray room, the patient inhaling some gases present in the air that were produced by the action of the high-tension current. Wilbert[3] expressed this same theory in a different manner as the cause of the symptoms. Another theory is that of a toxin produced in the blood by the roentgen rays and that this toxin is responsible for the blood changes causing roentgen ray sickness. (Linser and Sick,[4] Engel,[5] Joltrain and Bernard.[6])

Linser and Helber,[7] Warthin,[8] Rosenstern[9] and others have explained the symptoms upon a basis of a nephritis caused by the roentgen rays. Krause and Ziegler,[10] Buschke and Schmidt,[11] Hall and Whipple[12] could not find evidence of nephritis following roentgen ray treatment.

Lange[13] attributes the symptoms to the acidosis that develops as a result of cellular activity. Hirsch and Petersen[14] find a disturbance of the acid-base equilibrium, and sometimes a slight lowering of the alkaline reserve, manifested immediately after treatment of patients with roentgen rays. Golden[15] observed no diminution of the alkali reserve after treatment with roentgen rays.

Autolytic ferments present in tissues under normal conditions have been thought by some observers to be accelerated in their action as a

result of radiation (Baerman and Linser,[16] Rosenstern,[17] Edsall[18]). Heile[19] has shown that the spleen removed from dogs treated with radiation autolyses more rapidly than the control spleen from unrayed animals. Neuberg[20] found the same to be true using cancer tissue. Richards[21] experimented with ferments *in vitro* and found the roentgen rays in small doses accelerated and in larger doses inhibited action.

Some have thought the symptoms were brought about by the destruction of white blood cells with the liberation of the enzymes of theses cells.

The part played by ferments in the roentgen ray sickness must, at the present time, remain an open question. There is not sufficient experimental evidence to warrant a conclusion to be drawn at this time.

As mentioned above, the well known decrease in the number of white blood cells after treatment with roentgen rays has been connected in some way with roentgen ray sickness by several observers. Giraud, Giraud and Parès[22] have recently shown that the leucopenia does not follow the radiation of an organ (spleen) that has been clamped off from the circulation, but leucopenia occurs as soon as the clamps are removed and the blood of the treated organ is allowed to flow into the systemic circulation. The changes in the white blood cells following radiation would take us too far afield from our present paper to warrant further discussion at this time. But it might be added that the sensitiveness of the white blood cells, lymphocytes and leucocytes, is not limited to roentgen rays. These are probably the most responsive cells in the body as Leo Loeb[23] has recently stated: "They are the finest reagents for the discovery of what we have called syngenesio- and homotoxins."

Hall and Whipple[26] observed in dogs after massive doses of roentgen rays that the nonprotein nitrogen of the blood was markedly increased a short time before death, the urinary nitrogen increased following the exposure to the roentgen rays and remained high until the death of the animals. These authors conclude that the roentgen ray intoxication or general constitutional reaction is a good example of a "nonspecific" intoxication.

The chemical constituents cf the blood of cancer patients have received considerable attention. The first work was done in an effort to find some variations in these constituents that would help in understanding the neoplastic process involved or as an aid in its diagnosis. The results obtained from this line of work have been negative. (Theis[24, 25.])

There has been little attention paid to the blood from a chemical standpoint during the treatment of neoplastic growths with roentgen rays and radium. Whipple and his associates[26, 27] found an increase in the nonprotein and urea nitrogen of the blood in dogs exposed to massive doses of roentgen rays. These workers observed focal necrosis

in the lining of the small bowel and suggest that this may cause the general intoxication with the accompanying vomiting and diarrhea.

Hirsch and Petersen[28] could not demonstrate a striking or consistent alteration in the urea nitrogen, total nonprotein nitrogen, uric acid or creatinin in blood of carcinoma patients treated with roentgen rays.

The first effect produced upon the neoplastic growth after radiation is of a traumatic nature. The hyperemia that is first noted is quickly followed by an exudation of lymphocytes and leucocytes, and accompanying this one sees a swelling of the epithelial element in the radiated tumor.

There is always some necrosis in all malignant growths; there must be a process of autolysis going on all the time in such areas. Petry[29] was the first to call attention to this fact. This author found that the nitrogen not coagulated by heat is increased in breast carcinomata, while in the normal breast practically all of the nitrogen is coagulable. This has been substantiated by several workers.

If the proper amount of radiation energy is applied to a deep-seated neoplastic growth, the subsequent hyperemia and edema should lead to an increased absorption of the autolytic products. Noncoagulable proteins will form a part of the material in such an area. The absorption of these, with protein splitproducts of a higher order, within a relatively short period of time due to the hyperemia and increased permeability of the capillary plexus should lead to symptoms of intoxication in the patient.

If a larger dose of radiation is applied, leading to hemorrhage and thrombosis immediately following its application, we would expect little absorption from the radiated area as compared with one in which the dose was not great enough to damage the blood vessels in the area. Such an injury caused by overradiation should produce shock symptoms in the patient, not accompanied by evidence of absorption of the autolytic products of the neoplastic mass.

Freund and Kaminer[30, 31] found that tumor cells, separated from the connective tissue and blood, when suspended in 0.6 per cent sodium chloride solution, were destroyed by the serum of noncancerous subjects; but, on the other hand, they found serum of cancerous patients did not cause a destruction of the tumor cells in the suspension. They attributed this to some lytic property present in normal serum that was capable of destroying the cancer cells.

To review the whole field of the Freund-Kaminer reaction would take too much time and space. The results of various observers have not been constant. There are many uncontrollable factors involved in the reaction. I agree with most workers that this reaction can hardly be used for diagnostic purposes. My purpose in using the Freund-Kaminer reaction was to see the effect that would be exerted by the radiation

upon the serum of cancerous patients taken at various times following the initial therapeutic dose.

I wish only to mention the results obtained by other workers using the Freund-Kaminer reaction in malignant growths treated in various ways. Freund and Kaminer, using their original technic showed that the serum from patients who had the carcinoma removed by radical operative procedures, returned to the usual normal serum in respect to their lytic power of carcinoma cells. Koritschoner and Morgenstern,[32] by using the refractometric method, showed that in one case of carcinoma of the rectum the differences in the reading before and after digestion with the carcinoma cells and the patient's serum was –10; one month after the tumor was surgically removed, the difference was +20, or comparable to a normal serum. These authors also show two cases, five and four years respectively, after surgical removal of malignant growth, in which the sera reacted like nonmalignant or normal sera.

I have observed for many years a large number of patients with pelvic carcinomata subjected to radiation therapy. Some of these evidenced severe reactions, others showed only mild or no reactions at all. Again I lost seven patients who died from a severe intoxication. Clinically I found that patients having a clearly inoperable carcinoma with large ulcerating and infiltrating and necrotizing growths, usually showed a marked reaction, while the patients with borderline growths evidenced usually a mild or no reaction at all; while the deaths occurred in patients with frozen pelves and low vitality. The condition of the blood and leucopenia apparently did not explain these discrepancies in reactions. I therefore concluded to undertake a series of chemical analyses of the blood and blood serum to determine the effect of radiations on the patients.

The technic and dosage of radiation therapy have been described in other communications, especially in an article entitled "Technique and Statistics in the Treatment of Carcinoma of the Uterus and Contiguous Organs with the Combined Use of Radium and X-Rays," published in the *American Journal of Roentgenology* in October, 1922. Those interested are referred to this monograph to obtain the exact measuring of a 120, 150 or 175 per cent E.S.D. of combined radium and x-ray dosage.

To draw practical and clinical conclusions from these investigations I deemed it advisable to include in the list of cases investigated carcinomata of other regions of the body, and also benign uterine diseases subjected to radiation treatment.

TECHNIC

The patients entered the hospital at least twenty-four hours before the beginning of treatment. In most instances, they were in the hospital for a longer period of time before treatment was started. The

blood was taken from the arm vein before breakfast on the day the first radiation treatment was administered, the patient having been on a fluid diet for twenty-four hours. The next morning before breakfast another blood specimen was taken, the patient remaining on a fluid diet. The third specimen was taken one week after treatment; the fourth specimen six weeks after treatment. In many patients living at a distance from Chicago, it was impossible to obtain the fourth specimen as patients were dismissed from the hospital before this time after treatment. All blood specimens were taken before breakfast, i. e., during a postabsorptive period.

The blood chemical methods followed were those of Folin and Wu. The Freund-Kaminer[34] reaction was carried out according to the technic of those authors, using the refractometer suggested by Koritschoner.[33] The cancer tissue extract was obtained from Dr. G. Kaminer.

Table I contains in brief tabulated form the record of thirty-five cases studied by us during the past few months. The blood chemical findings: (1) before treatment; (2) twelve to eighteen hours after treatment; (3) one week after treatment; and (4) six weeks after treatment. There is, in addition to diagnosis, a short note of the outstanding features of the condition with the dose of radiation energy used.

Cases of carcinoma of the cervix of the uterus showing intoxication following radiation treatment. Cases I to VII inclusive.

Reference to Table I will show that all seven cases included in Table II are advanced carcinomata of the cervix; parametrium and vagina were invaded in most instances. Necrosis was present in all cases, usually most marked in the cervix, surrounded by the malignant and infiltrating growth. Intoxication followed the radium treatment.

The average nonprotein, urea and rest nitrogen before treatment are within the normal amounts found in resting individuals on a fluid diet. Even the increase after radiation is not high for blood under pathologic conditions, but is 40 to 55 per cent higher than before treatment.

Cases of carcinoma of organs other than the uterus, with one case of myoma uteri, showing intoxication following radiation treatment. Cases VIII to XIV inclusive.

Upon consulting Table I, it will be seen that the cases referred to in Table III can hardly be considered together from a morphologic or pathologic standpoint. Two were mammary cancer, one bladder, one lingual, one lip cancer, one inguinal lymph gland, involvement by metastasis from scrotum cancer, and one was myoma of the uterus. There was one feature characterizing all of these growths, namely, degenerative processes. Intoxication followed the radiation treatment.

When Table III is examined, it will be seen that the amounts of the various nitrogen fractions are higher before treatment than are those cases considered in Table II; in fact, the average normals in Table III are about the same as the average after treatment figures in Table II.

TABLE I

PATIENT	DIAGNOSIS		BLOOD CHEMICAL ANALYSIS						REACTION FROM RADIATION	REMARKS
			N. P. N.	UREA	CREATININ	URIC ACID	REST N.	SUGAR		
Mrs. S. I	Carcinoma cervicis uteri	I II III IV	21.1 38.8 29.0 26.1	11.0 18.6 15.0 13.8	2.2 2.1 2.5 1.8	2.2 3.4 3.0 2.8	5.7 14.7 8.5 7.7	0.11 0.08 0.14 0.07	Severe	Cervix filled with soft tissue. Paracervical infiltration. 175% E.S.D.
Mrs. C. II	Carcinoma cervicis uteri	I II III IV	34.7 38.2 22.2 22.9	17.1 19.0 11.0 9.9	1.6 1.7 1.2 1.5	3.0 3.1 2.9 2.7	13.0 14.4 7.1 8.8	0.06 0.09 0.06 0.07	Severe	Cervix filled with necrotic mass. Parainfiltration. 100% radium dose.
Mrs. N. III	Carcinoma cervicis uteri Diabetes mellitus	I II III IV	31.2 38.4 28.4 23.1	16.0 19.0 15.6 12.7	1.6 1.6 1.5 1.2	2.9 3.0 2.8 3.0	10.7 14.8 8.5 6.2	0.13 0.14 0.13 0.13	Severe	100% radium dose.
Mrs. C. IV	Carcinoma cervicis uteri recurrens	I II III IV	30.7 40.2 27.0 23.8	15.1 20.6 14.8 11.7	1.5 1.9 1.5 1.5	1.4 2.1 1.8 1.8	12.7 15.6 8.9 8.9	0.08 0.09 0.07 0.08	Severe	Vagina and parametrium invaded. 150% E.S.D.
Mrs. T. V	Carcinoma cervicis uteri	I II III	25.7 40.9 32.0	14.0 21.2 17.2	1.2 1.4 1.3	3.0 3.3 2.8	7.5 15.0 10.7	0.14 0.12 0.08	Severe	Infiltration of whole cervix. No parametrial involvement. 120% E.S.D.
Mrs. H. VI	Carcinoma cervicis uteri	I II III	21.0 33.8 31.3	12.0 18.0 18.0	1.2 1.5 1.4	4.2 4.9 3.6	3.6 9.4 8.3	0.12 0.14 0.09	Severe	Cervix filled with necrotice mass. Paracervical invasion. 175% E.S.D.
Mrs. P. VII	Carcinoma cervicis uteri	I II III IV	22.8 35.3 25.8 26.1	10.0 17.6 12.4 14.0	1.0 1.1 1.0 1.1	3.5 4.1 3.0 3.0	8.8 12.5 11.4 8.8	0.09 0.09 0.09 0.10	Severe	Vaginal wall and parametrium involved. 150% E.S.D.
Mrs. W. VIII	Carcinoma mammae recurrent	I II III	32.6 43.3 35.6	17.4 21.2 18.0	2.1 2.4 2.3	3.4 4.2 4.1	9.7 15.5 11.2	0.12 0.14 0.13	Severe	Lung involvement. 150% E.S.D.
Mr. B. IX	Carcinoma inguinal glands	I II III	35.2 42.3 35.8	18.0 20.0 18.6	2.5 2.6 2.4	3.0 2.9 3.1	11.7 16.8 11.7	0.06 0.06 0.06	Severe	Recurrent from carcinoma of scrotum. Sloughing and necrotic mass. 175% E.S.D.
Mr. F. X	Carcinoma tongue	I II III IV	42.3 48.1 38.4 31.6	20.7 23.8 18.4 16.0	1.7 1.6 1.2 1.5	4.4 4.5 4.0 4.4	15.5 18.2 14.8 9.7	0.10 0.11 0.10 0.10	Severe	Large ulcerating and necrotic mass on left side, involving tonsil and pharynx. 150% E.S.D.
Mrs. C. XI	Carcinoma bladder	I II III	37.1 51.6 43.8	19.3 25.4 21.0	2.5 2.7 2.4	3.0 4.5 4.1	12.3 19.0 16.3	0.12 0.16 0.14	Severe	100% radium dose. 120% x-ray dose.
Mrs. S. XII	Carcinoma mammae	I II III	32.6 68.4 44.0	20.4 39.6 26.2	2.3 3.3 2.9	3.5 3.8 3.5	6.4 21.7 11.4	0.11 0.12 0.11	Severe	Infiltrating growth involving both breasts. 175% E.S.D.

TABLE I—Cont'd

PATIENT	DIAGNOSIS		BLOOD CHEMICAL ANALYSIS						REAC-TION FROM RADIA-TION	REMARKS
			N. P. N.	UREA	CREATININ	URIC ACID	REST N.	SUGAR		
Mrs. V. XIII	Myoma uteri	I	36.3	19.1	2.2	3.0	12.0	0.14	Severe	Necrotic areas in myoma. 100% radium dose.
		II	52.1	27.0	1.8	3.2	22.1	0.15		
		III	39.9	21.0	1.9	3.0	14.0	0.13		
Mr. R. XIV	Epithelioma lower lip	I	36.3	19.4	3.6	4.1	9.2	0.11	Severe	Ulceration and involvement of cervical lymph nodes.
		II	44.0	20.6	3.4	3.9	16.1	0.13		
		III	38.2	18.2	3.0	3.7	13.3	0.10		
		IV	30.6	16.1	3.1	4.0	7.4	0.10		
Mrs. C. XV	Carcinoma mammae	I	28.8	14.7	1.3	3.0	9.8	0.09	None	Superficial ulceration. No involvement of axilla, etc. 150% E.S.D.
		II	26.3	13.7	1.4	3.1	8.1	0.11		
		III	24.8	12.5	1.3	3.2	7.8	0.10		
Mrs. P. XVI	Carcinoma mammae	I	42.9	22.1	2.1	3.2	15.5	0.11	None	Superficial ulceration. No involvement of axilla, etc. 175% E.S.D.
		II	47.3	24.2	2.3	4.0	16.8	0.12		
		III	29.1	15.0	2.1	3.8	8.2	0.12		
Mrs. R. XVII	Carcinoma cervicis uteri	I	20.6	9.8	1.6	1.7	7.5	0.09	Slight	Cervix amputated. Uterus and adnexa normal. 130% E.S.D.
		II	25.1	12.1	1.5	1.6	9.4	0.10		
		III	24.7	11.3	1.8	1.8	9.8	0.09		
Mrs. B. XVIII	Chorio-epithelioma	I	32.9	17.0	1.5	2.8	11.6	0.11	None	Removed with curette. 175% E.S.D.
		II	40.5	22.4	1.4	3.7	13.0	0.10		
		III	37.3	19.3	1.6	3.8	12.6	0.09		
Mrs. Z. XIX	Sarcoma of Corporus uteri	I	25.4	12.0	2.0	3.9	7.5	0.10	None	150% E.S.D.
		II	24.2	12.6	1.5	2.4	7.7	0.11		
		III	23.0	11.8	1.6	3.3	7.3	0.10		
Mr. B. XX	Carcinoma of tonsil	I	31.7	17.4	1.5	3.0	13.1	0.09	None	150% E.S.D.
		II	30.0	16.2	1.3	3.1	9.4	0.10		
		III	26.0	16.6	1.5	2.9	5.0	0.09		
Mr. F. XXI	Carcinoma right antrum	I	25.9	13.0	1.8	2.7	8.4	0.08	None	Curetted. 150% E.S.D.
		II	28.0	14.0	2.0	3.0	9.0	0.10		
		III	30.4	16.8	2.0	2.9	8.7	0.08		
Mr. P. XXII	Carcinoma lower jaw	I	30.3	12.8	1.5	3.8	12.2	0.12	None	Solid hard tumor mass. 150% E.S.D.
		II	32.0	16.4	1.4	4.0	10.2	0.14		
		III	37.0	18.1	2.2	3.6	13.1	0.14		
Mrs. M. XXIII	Hemorrhagic metropathy	I	25.6	14.0	1.5	2.4	7.7	0.10	None	100% E.S.D.
		II	19.1	10.0	1.6	3.0	4.5	0.11		
		III	25.9	13.6	1.7	2.9	7.7	0.10		
Mrs. M. XXIV	Hemorrhagic metropathy	I	28.0	13.5	1.9	1.9	10.7	0.09	None	75% E.S.D. radium intrauterine. 100% E.S.D. x-ray.
		II	32.0	17.0	1.6	2.4	11.0	0.10		
		III	23.7	12.0	1.4	2.0	8.3	0.08		
Mrs. P. XXV	Hemorrhagic metropathy	I	35.2	17.0	1.8	2.0	14.4	0.06		100% E.S.D.
		II	36.2	18.0	2.0	2.2	14.0	0.06		
		III	32.1	16.0	1.8	2.1	12.2	0.05		
Mrs. M. XXVI	Carcinoma cervicis uteri	I	27.6	12.1	2.6	2.1	10.8	0.09	Slight	3 months previous had 100% E.S.D. 175% E.S.D. at this time.
		II	26.1	14.2	3.0	2.4	8.4	0.10		
		III	26.0	11.0	2.8	2.2	10.0	0.10		

TABLE I—Cont'd

PATIENT	DIAGNOSIS		BLOOD CHEMICAL ANALYSIS						REACTION FROM RADIATION	REMARKS
			N. P. N.	UREA	CREATININ	URIC ACID	REST N.	SUGAR		
Mrs. K. XXVII	Carcinoma cervicis uteri	I II III	23.5 24.4 22.0	13.6 15.1 12.0	2.1 2.0 2.2	3.9 4.0 3.7	3.9 3.3 4.1	0.10 0.10 0.09	None	4 months previously had 175% E.S.D. Large infiltrating mass in left parametrium. 175% E.S.D.
Mrs. B. XXVIII	Carcinoma cervicis uteri	I II III	31.5 33.3 30.1	18.2 16.1 17.3	2.1 2.0 2.0	1.9 2.1 2.0	9.7 13.1 8.8	0.10 0.11 0.09	Slight	Extensive recurrence with necrosis. Previously treated with x-ray.
Mrs. D. XXIX	Metastatic tumor anterior abdominal wall	I II III IV	29.9 27.5 23.4 28.0	16.4 12.0 13.6 14.7	2.6 2.5 2.4 2.5	3.1 3.0 2.8 3.0	7.8 10.0 4.6 7.8	0.09 0.10 0.11 0.09	None	Following oophorectomy for cystoma. Treated 7 months previously with x-ray.
Mrs. P. XXX	Carcinoma cervicis uteri	I II III	30.7 29.6 28.7	15.6 14.4 14.0	2.4 3.0 2.8	3.1 3.4 3.2	9.6 8.8 8.7	0.10 0.10 0.09	None	Ulceration and necrosis marked. Radiated 5 months previously.
Mr. C. XXXI	Carcinoma right inferior maxilla	I II III IV	25.4 24.4 26.0 20.0	12.2 11.8 13.7 9.2	3.8 3.9 3.5 2.3	4.0 4.1 3.3 3.5	5.4 4.6 5.5 5.0	0.12 0.13 0.12 0.09	None	Necrosis and cervical glands involved. Terminal. 150% radium dose.
Mrs. N. XXXII	Carcinoma cervicis uteri recurrens	I II III	25.4 30.2 29.5	12.1 16.0 14.7	2.5 2.6 2.3	2.1 2.0 2.1	8.7 9.6 10.4	0.07 0.09 0.08	None	Pelvis frozen. Vaginal vault necrotic. Terminal. 175% E.S.D.
Mr. F. XXXIII	Carcinoma cervical glands	I II III	36.1 27.4 29.5	20.8 11.9 15.4	2.2 2.0 1.8	3.0 3.3 2.9	10.1 10.2 9.4	0.09 0.08 0.08	None	Large indurated area. Terminal.
Mrs. R. XXXIV	Carcinoma mammae recurrens	I II III IV	20.6 48.3 31.7 37.9	9.6 24.0 15.3 14.0	3.6 4.2 3.9 2.3	4.0 4.6 3.8 4.0	2.8 15.5 8.7 7.9	0.10 0.11 0.09 0.11	None	Radical amputation 6 months previous. Scar and axilla indurated. 150% E.S.D.
Mr. D. XXXV	Metastatic carcinoma kidney	I II III	24.6 28.9 27.4	16.3 19.3 17.2	2.6 2.1 2.4	3.6 4.2 4.0	2.1 3.3 3.8	0.10 0.09 0.10	Slight	130% x-ray dose.

The amounts of nitrogen in the blood after treatment in the group included in Table III are too high to be considered normal. The increase in the nonprotein and urea nitrogen was 33 and 32 per cent, but the rest nitrogen fraction increased 96 per cent.

The high control nonprotein fractions are suggestive of kidney impairment in this series. The increase in the nonprotein and urea nitrogen in the blood after treatment is not so great as the increase in the rest nitrogen fraction; the latter increased almost 100 per cent as compared with 33 per cent of the former two respectively. This is prob-

TABLE II

| | BEFORE TREATMENT | | 12 TO 18 HOURS AFTER TREATMENT | | |
	VARIATIONS	AVERAGE	VARIATIONS	AVERAGE	INCREASE
Nonprotein nitrogen	21.0-34.7*	26.7	33.8-40.2	37.9	42%
Urea nitrogen	10.0-17.1	13.6	17.6-21.2	19.1	40%
Rest nitrogen	3.6-13.0	8.8	9.4-15.6	13.7	55%

*All figures represent milligrams per 100 c.c. whole blood.

TABLE III

| | BEFORE TREATMENT | | 12 TO 18 HOURS AFTER TREATMENT | | |
	VARIATIONS	AVERAGE	VARIATIONS	AVERAGE	INCREASE
Nonprotein nitrogen	32.6-42.3*	36.0	42.3-68.4	47.1	33%
Urea nitrogen	17.4-20.4	19.2	20 -39.6	25.4	32%
Rest nitrogen	6.4-15.5	9.5	15.5-22.1	18.5	96%

*All figures represent milligrams per 100 c.c. whole blood.

ably due to the increased absorption of autolytic products present in and around the tumor areas exposed to radiation.

The severe cases of ''roentgen ray sickness'' were encountered in this group of cases of early neoplastic growths of various organs not showing intoxication following radiation treatment.

Cases of early neoplastic growths of various organs not showing intoxication following radiation treatment. Cases XV to XXII inclusive.

The cases considered in Table IV form a varied pathologic group. They were all early neoplastic growths, characterized by little or no evidence of degenerative changes. No intoxication was noticed after radiation. The nitrogen fractions, as shown in Table IV, before and after treatment do not show a marked change, the fluctuations are within normal daily variations, the changes varying from +9 to –14 per cent.

TABLE IV

| | BEFORE TREATMENT | | 12 TO 18 HOURS AFTER TREATMENT | | |
	VARIATIONS	AVERAGE	VARIATIONS	AVERAGE	INCREASE (+) OR DECREASE (−)
Nonprotein nitrogen	20.6-42.9	29.8	24.2-47.3	31.6	+6%
Urea nitrogen	9.8-22.1	14.8	12.6-24.2	16.3	+9%
Rest nitrogen	7.5-15.5	10.7	7.7-16.8	9.2	−14%

Cases of hemorrhagic metropathy; no intoxication following radiation. Cases XXIII to XXV inclusive.

There was little variation in the blood nitrogen fractions before and after treatment in these cases. (Table I.) It should also be noted that the dosage was small as compared to that used for therapeutic doses in malignancy. In these cases the necrotic or autolyzing tissue was negligible in amount and the dosage was in keeping with the minor pathologic changes.

The results of the blood chemical findings in these and subsequent cases does not warrant special tabulation; such tables would not differ materially from the averages shown in Table IV.

Recurrent cases of malignancy following previous treatment by radiation. There was no intoxication in these cases after the last treatment. Cases XXVI to XXX inclusive.

The nitrogen fractions do not show much variations before and after treatment in these cases. There was no intoxication following our treatment.

Very advanced cases of malignancy showing no evidence of intoxication after radiation. Cases XXXI to XXXIII inclusive.

These were all hopeless cases. The absence on any evidence of a reaction although autolysis and other degenerative changes were present, we attribute to lack of reactive power on the part of the patient. All of these cases died within a short period of time.

CASE XXIV.—Carcinoma of right breast; radical amputation on September 5, 1922. On December 28, 1922, the area of operation, scar and the axilla were found indurated. Several palpable nodules were in the chest wall. It was radiated with 175 per cent E.S.D. There was a marked rise in the various nitrogen fractions of the blood after treatment. There was no intoxication accompanying this rise. In this respect this case is an exception to the previously mentioned cases. We cannot explain this lack of reaction accompanied by a marked elevation of the nonprotein nitrogen fractions at this time. We cite this case as an exception to those recorded above.

CASE XXXV.—Metastatic carcinoma of the left kidney. A large massive tumor was felt in the upper left abdomen surrounded by indurated area. Two operations had been previously performed for the removal of the tumor in this region, one five years and one three months before applying for treatment. A 130 per cent E.S.D. of x-rays was given. There was no marked intoxication and no change in the nonprotein nitrogen constituents comparable to other cases of similar nature. I cite this case as another exception to those reported in this paper.

I have omitted all cases of malignancy treated by radiation that show abnormally high nonprotein nitrogen of the blood. These cases have severe kidney involvement of one kind or another and cannot be considered in this group. I am engaged in the study of this type of cases at the present time.

The results obtained by radiation in experimental laboratory animals is hardly comparable with those obtained by radiation in cancer patients. The size of the field of radiation, the anatomic location, the histologic structure, the chemical composition and the vascularity of the tumor mass all must be considered, in conjunction with the proper dosage of radiation energy, before we can interpret the immediate and latent action arising in the patient.

The patients showing a severe reaction following the treatment with roentgen rays and radium have an increase in the nonprotein nitrogen of the blood. The urea and the rest nitrogen fractions show the greatest

increase in amounts. I think this is due to rapid absorption of the autolytic products from the tumor area, due to the hyperemia and edema that follow immediately after radiation.

The increase in uric acid is more marked, as a rule, than the creatinin; this, I think, comes from the same source.

The patients showing no evidence of intoxication did not have a noticeable increase in the nonprotein nitrogen of the blood.

"Radiation sickness" occurs in those patients who have areas of autolyzed or necrotic tissue associated with the neoplastic tumors. This reaction comes on relatively soon after radiation. The microscopic picture of the tumor at the time "radiation sickness" occurs in the patient shows an inflammatory reaction primarily. The hyperemia of the blood vessels with edema of the adjacent tissues is a characteristic picture. The degnerative changes in the neoplastic cellular tissue is not noticeable at this time, but occurs five to seven days after radiation.

The following examples, cases taken from Table I, can be cited and used to make clearer the above statement.

Mrs. C.—II. Necrotic mass in the cervical region; parametrium infiltrated. Received 100 per cent E.S.D. Severe intoxication.

Mrs. T. V.—Infiltration and ulceration of the cervix; no parametrium involvement. Received 120 per cent E.S.D. Severe intoxication.

Mrs. B.—XVIII. Chorioepithelioma, removed with curette. Received 175 per cent E.S.D. No intoxication.

Mrs. R.—XVII. Early carcinoma of the cervix; uterus and adnexa normal. Cervix amputated fourteen days before radiation began. Received 130 per cent E.S.D. No intoxication.

A careful study of Table I reveals many such instances. In these four cases just mentioned, the first two received less radiation than the third case, although the former two had "radiation sickness," the latter case showed little or no evidence of intoxication. The first and fourth cases just cited were both cervical carcinoma, the one with the autolyzing masses of tissue had severe "radiation sickness;" the latter one with no evidence of any degenerative process in pelvis, did not show evidence of intoxication.

Necrotic or autolyzing areas of tissue, particularly when parenchymal elements predominate, are always acid in reaction. The increased hydrogen-ion concentration of the part, due to the interaction of many factors, such as decreased oxygen supply, increased carbondioxide tension, organic acid radicals, accumulates as a result of excessive catabolic activity in such an environment and probably plays some minor rôle in the "radiation sickness" after absorption of these acid products. A slight shifting of acid base equilibrium in the blood after radiation of cancer patients would be expected; that this should be of short duration and quickly corrected by a mobilization of alkali reserve would also be expected under physiologic conditions. An overcorrection, by the mobil-

ization of more alkali than necessary to just balance the acid bodies absorbed, would also be expected to take place under physiologic conditions. This is exactly what Hirsch and Petersen[14] found to be true by careful experiments, using the gas chain method to obtain the hydrogenion concentration values of the blood of cancer patients before and after radiation.

The conclusions and clinical significance to be drawn from these observations are: (1) Patients with carcinomata free from necrosis and of limited extent called localized and borderline cases may be given the total radiation dose within the shortest time possible. (2) Patients with extensive and necrotizing carcinomata should be treated with fractional doses at stated intervals. We may apply at the first sitting a dose which will arrest the bleeding and discharge, and temporarily stem the further growth of the carcinoma. As soon as the patient has passed the period of the radiation intoxication the rest of the dose may be applied. We thus ameliorate the distressing symptoms and stormy course of the radiation intoxication. (3) Patients with extensive carcinoma filling the small pelvis, having large necrotizing masses and causing advanced cachexia should not be subjected to radiation treatment. They cannot be benefited in the slightest degree and we only hasten the inevitable fatal end. (4) Recurrences occurring after the application of a correctly gauged radiation dose should not be retreated. Such patients have become radiation fast. A useless repetition of the treatment must effect a distrust in an otherwise valuable treatment.

TABLE V

		SERA BEFORE ADDING TO TISSUE		SERA 45 MINUTES AFTER ADDING TO TISSUE		SERA 24 HOURS AFTER ADDING TO TISSUE		DIFFERENCE
		READING	N.D.	READING	N.D.	READING	N.D.	
Average of 12 normal sera		61.5	1.35076	61.5	1.35076	61.8	1.35088	12
Mrs. A.	I	56.4	1.34888	56.4	1.34888	56.4	1.348888	0
Carcinoma of	II	55.8	1.34865	55.8	1.34865	55.8	1.34865	0
cervix uteri	III	55.15	1.34842	55.15	1.34842	55.1	1.34840	−2
	IV	56.2	1.34880	56.2	1.34880	56.4	1.34880	+8
Mrs. T.	I	58.0	1.34947	58.0	1.34947	58.1	1.34950	+3
Carcinoma of	II	56.2	1.34880	56.2	1.34880	56.5	1.34891	+11
cervix uteri	III	57.1	1.34914	57.1	1.34914	57.6	1.34932	+18
	IV							
Mrs. B.	I	63.4	1.35147	63.4	1.35147	63.4	1.35147	0
Carcinoma of	II							
right breast	III	62.0	1.35095	62.0	1.35095	59.5	1.35103	+8
	IV							
Mr. B.	II	55.0	1.34836	55.0	1.34836	55.0	1.34836	0
Carcinoma of	II							
left ear	III	54.6	1.34820	54.6	1.34820	54.8	1.34828	+8
	IV							
Mrs. H.	I	60.4	1.35036	60.4	1.35036	60.4	1.35032	−4
Carcinoma of	II	59.3	1.34995	59.3	1.34995	59.7	1.35010	+15
cervix uteri	III	59.5	1.35002	59.5	1.35002	59.8	1.35024	+22
	IV							

Table V gives in condensed form the results obtained by using the Freund-Kaminer reaction on the serum of carcinoma patients treated with radium and roentgen rays. The Roman figures on the margin designate the time in relation to the treatment that the serum was obtained: (I—before treatment; II—twenty-four hours after treatment; III—seven days after treatment; IV—four weeks after treatment.)

The technical difficulties encountered in the refractometric Freund-Kaminer reaction are so great that the use of this reaction is limited in its value. Outside of the usual precautions for such refractometric work, the repeated handling of the sera under strictly sterile conditions is very difficult. All experiments were run in triplicate. All readings made upon sera that showed cloudiness or bacterial growth upon subculture were eliminated.

An examination of the cases reported upon will show a gradual change toward normal serum reaction after treatment with radium and roentgen rays. This is the same as has been observed by other authors after surgical removal of malignant growths.

This report is a preliminary publication upon this subject. The chemical study of the blood is now being continued, and will be extended to a careful metabolic study of the patients treated with radiation. The Freund-Kaminer reaction is also being extended to include the patients studied from the above mentioned standpoint.

SUMMARY

1. "Radiation sickness" is caused by the absorption of autolytic products from the degenerative areas of the tumor mass. This intoxication is an example of a "nonspecific" reaction.

2. The sera of patients with carcinoma become carcinomalytic after treatment with radium and roentgen rays, as evidenced by the Freund-Kaminer reaction.

3. The results of the chemical and serum examinations of the blood of carcinoma patients would indicate that patients with extensive and necrotic cancer tumors should be subjected to radiation therapy with a great deal of caution, using preferably a fractional interval method to prevent severe radiation intoxications. Patients with advanced carcinomata should not be subjected to radiation therapy.

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MENINGEAL HEMORRHAGES OF THE NEWBORN AND THEIR REMOTE CONSEQUENCES*

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FROM the very onset of embryonic life up to the period of birth, the fetus is exposed to multiple damaging influences which have a direct bearing upon the growth of its central nervous system. Lesions of the latter may be numerous and various with regard to their localization, extent, and depth. They are apt to compromise the cerebral functions not only at the time the damage is done but especially during later development of the nervous system. If the infant survives, infirmities are seen not only in the sensori-motor sphere but also and particularly in the mental faculties in which a definite defect is manifest. Among all the multiple facts which are apt to lead to such consequences, only meningeal hemorrhages at birth will be discussed here.

During birth hemorrhages may occur at different levels, either within the nervous tissue itself or close to the cranium. In the latter case the blood may be located between the bone and its periosteum (cephalhematoma), between the periosteum and the dura, or else beneath the dura.

In order to understand the mechanism of formation of hemorrhagic foci, a brief account of the anatomic arrangement of the membranes with their vascular supply is necessary.

The dura mater consists of two layers, an inner and an outer. The outer, which is the periosteal membrane, sends septa into the cranial

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cavity accompanied by venous sinuses. They are the falx cerebri, which encloses the superior and inferior sagittal sinuses, also the straight sinus along the line of junction of the base of the falx with the tentorium, the tentorium cerebelli with the transverse and superior petrosal sinuses and the falx cerebelli with the occipital sinus. The septa are in certain places reinforced by aggregation of fibrous bands which enable the head to withstand the great strain in delivery.

During a difficult labor the frequent changes in the shape of the head and the excessive tension overstretch the septa and tears follow which may be complete or incomplete, unilateral or bilateral. When the tentorium cerebelli is involved, the tear is usually found below its junction with the falx. When the falx cerebri is damaged, the tear occurs at the level of its middle two-thirds. Holland[1] found in a series of 167 cases tears in tentorium in 48 per cent and in all of the latter subdural hemorrhages. The fine blood vessels and the large vein on the border of the small circumference of the tentorium may be the sources of hemorrhage, although the usual origin is in the tributaries of the vein of Galen received from the cerebellum and midbrain and from the cerebellar veins entering the straight sinus. The experimental investigations of Holland prove this contention conclusively. These tributary veins are stretched between the fixed point of the Galen vein and the fixed cerebellum. During the excessive tension in difficult labor the apex of the tentorium is drawn upwards and consequently the vein of Galen is twisted at its entrance into the sinus; an enormous distention of this vein and of its tributaries follows. On the other hand the cerebellum is at that time pressed down into the posterior fossa by the undue pressure of the occipital lobes of the brain. Under such circumstances the fine veins tributary to the Galen vein as well as the cerebellar veins entering the straight sinus rupture.

Over the surface of the cerebral hemisphere similar subdural hemorrhages may occur during difficult labor, and it is particularly intense in breech presentations. A common form of such an occurrence is between the layers of the falx cerebri, although less frequent than in tentorial cases. Occasionally there may be a hemorrhage at the base of the brain. Rarely does the pia arachnoid tear but in such cases small hematomata occur. Ventricular hemorrhages, although rare, may nevertheless occur from extreme distention of the fine veins of the choroid plexuses.

The seat of hemorrhages is of importance. In the tentorial cases, for example, even a small blood effusion beneath the tentorium would be of graver consequence than one on its surface however large it may be. Tears in the tentorium cerebelli are the most common and

those of the falx cerebri are rather rare, and in the majority of cases to be found in association with tears in the tentorium.

In considering the causation of meningeal hemorrhages it is extremely important to bear in mind the immediate and the predisposing factors. Infections and intoxications *in utero* may be the direct cause, but the most frequent one is traumatism during labor, extraction of the head in breech cases, forceps delivery for contracted pelvis, presentation of the face or forehead. Tearing of the tentorium has been found in about 70 to 75 per cent of dead fetuses delivered by the breech. Holland, however, believes that in such cases the tentorial condition was due to rapid delivery after version, but if breech delivery is properly managed, there should not be sufficient intracranial tension to produce tearing of the tentorium. The same view can be applied to the cases with transverse presentation. Circulatory interference in the umbilical cord, and congenital malformations of the central nervous system are also not infrequently the cause of intracranial hemorrhages.

The frequency of meningeal hemorrhages in the newly born can be noted in the statistics of G. Hedren of Stockholm,[2] and of Cruickshank.[3] The former examined 700 infant cadavers and found intracranial hemorrhages in about 9.28 per cent. The bleeding was restricted to the meninges in nearly 84 per cent, and cerebral hemorrhage accompanied by meningeal hemorrhage in others brings the total of meningeal hemorrhages to 90.7 per cent. Delivery had been spontaneous in 50 of the 65 cases, and the conditions in both mother and child seemed to be normal in most of the cases. In the 42 purely meningeal cases, the hemorrhage had been supratentorial in 32, infratentorial in 10 and both in six. An analysis of these cases leads to the conclusion that intracranial hemorrhages may occur with rapid and easy spontaneous delivery and they may occur without fractures.

In Cruickshank's account of 200 cases one finds an incidence of 65 cases which showed meningeal hemorrhages of a gross character. In 25 cases there was meningeal hemorrhage associated with hemorrhage into the viscera.

Clinical Manifestations.—Meningeal hemorrhage is more frequently suspected than actually determined during life. Death may ensue in a few hours following the meningeal hemorrhage, but if the infant survives, one observes a state of apparent collapse, cyanosis, low temperature, convulsions in the subsequent days, circulatory and respiratory disturbances, various palsies and contractures. When the infant further succeeds in overcoming the immediate effect of the bleeding the above stormy symptoms gradually subside and the child enters into a chronic state of physical and mental inferiority with a crippled central nervous system. Diplegia, hemiplegia, spastic paraplegia, contractures, athetosic or choreiform movements, convulsive phenomena,

amaurosis, mental deficiency or debility of various degrees, constitute a symptom group which could be placed under one caption of "infantile encephalopathies." Of course, this vast group presents various degrees in its extent and intensity. There are mild cases and profoundly damaged cases. From the standpoint of intellectual development the child may be an idiot or an imbecile or may present only a slight degree of mental arrest of development. It all depends upon the hemorrhage and upon the facility with which the blood may be absorbed or otherwise removed.

The encephalopathies may be early or precociously diffuse, which leads to idiocy; they may be late or delayed, circumscribed and frequently slight which in adult life will be manifested in but slight disturbances of intelligence. The arrest of intellectual development will be especially pronounced and less amenable to improvement in those cases which through hereditary factors are inevitably predisposed to, and prepared for, disturbances or anomalies of cerebration.

A brief physiologic consideration is warranted:

At birth the cells of the central nervous system are fully developed. As to the nerve fibers, full growth is present only in those which control reflex movements, circulation, respiration, and nutrition. The nervous mechanisms of the spinal cord and medulla alone are functionating at that period of life. On the other hand the fibers originating in the frontal, rolandic, occipital, parietal, temporal regions of the brain, as well as the projection and commissural fibers, become myelinated only some time after birth. It is therefore evident that early symptoms will be only those which are in relation to the physiologic function of the medulla and spinal cord, but manifestations depending upon the function of various portions of the brain will be in evidence ulteriorly and for the above reasons will remain permanent. If we add the compression of the convolutions exercised by the blood, also the possibility of breaking up of the cerebral tissue and infiltration of the latter with the blood, the physiologic damage is then easily conceived.

A brief description of the several clinical varieties may be helpful for a full understanding of hemorrhagic possibilities.

1. *Cerebral Diplegia.*—Two important subvarieties should be considered, one the classical Little's disease, in which there is a spastic paraplegia of the upper and lower extremities, the spasticity being more pronounced than the paralysis, but in which there are no convulsive phenomena and the intelligence is preserved. Improvement is a common occurrence. This form is fundamentally of agenesic order and due to a congenital insufficiency of the pyramidal tract. Premature birth is the original cause.

The second variety is due to destructive lesions of an inflammatory or traumatic origin from a difficult delivery. Here the motor areas

as well as other portions of the cortex, are usually involved, thus producing besides spasticity and paralysis also serious convulsive phenomena and disturbance of intelligence. The condition is persistent. The clinical picture of the last form of cerebral diplegia will vary according to the predominance of involvement of different areas. The association of intellectual phenomena with paralysis and spasticity of the limbs indicates a lesion in the frontal and rolandic areas. Here one or the other may predominate but the presence of epileptiform manifestations is always an unfavorable condition for the intellectual development and in all such cases the mental deficit is much pronounced. Athetosic and choreic movements are also frequently observed in this variety of diplegia.

An interesting feature of the intellectual status in the first variety of diplegia deserves special mention. There is a striking discord between the appearance of the little patients and the real state of intelligence. At first glance the difficult speech and the expression of the face with the mouth open may suggest a low mental state, but an actual test and close observation of their behavior and of their relation to the environment will reveal an integrity of intelligence.

The difference consequently between the two forms of diplegia is fundamental and its second variety is by far more serious than the first. Since it is due to obstetric traumata, the danger of meningeal hemorrhages in difficult labor, cannot be overestimated.

2. *Cerebral Hemiplegia.*—Should the hemorrhage be limited to one hemisphere, hemiplegia with all its characteristics will be the result. In almost all such cases intellectual deficiency is more or less pronounced; all degrees between ordinary mental arrest and idiocy are observed. The inequality and irregularity in the intellectual deficit are due to the great variation in the extent and intensity of the lesions in one hemisphere. As to the hemiplegia itself, it differs from that in an adult, as, in addition to the paralysis, there is considerable lack of development of the affected limbs; they are small not only with regard to the musculature but also to the bony tissue; there are permanent contractures with secondary deformities, hemiathetosic and hemichoreic movements, also frequently aphasia is absent in cases of right hemiplegia.

Not infrequently alongside and in place of complete or incomplete intellectual obliteration other spheres of sensory-psychic activity are developed, but close analysis will reveal that the latter are only of a purely reflex character, are automatic and lack in associative integration, and therefore lose all psychic value.

3. *Double Athetosis and Athetoso-Choreic Movements.*—Encephalopathies in infants may be manifested by a more or less marked deficit in the intellectual sphere and accompanied by bilateral motor phenomena in the form of chorea or athetosis. Here again various de-

grees of involvement may be present; there are cases with very slight disturbances in the psychic sphere, in which on the contrary the motor manifestations are most conspicuous. There are cases in which the two conditions are reversed. They are all observed in infants in which instrumental deliveries were done.

The three forms of encephalopathies described are the extreme and gross types. There are many intermediary forms which depend upon the portion of the brain affected by the meningeal hemorrhage. Thus any portion of the rolandic area may be affected; the centers of the leg, arm, or face, lips, tongue may be individually compressed. There are cases with a minimum of diplegia; cases with pseudobulbar manifestations; speech defects showing involvement of the speech centers, motor or sensory; exclusive mental defect indicating an involvement of the frontal lobes; persistent and frequent epileptiform convulsions in which particularly the mental development suffers the most, and finally there may be cases with unilateral or bilateral cerebellar manifestations, the so-called cerebellar hemi- or diplegia types, in which cerebellar manifestations alone are conspicuous.

CONCLUSIONS

On the preliminary pages it was mentioned that the causes of meningeal hemorrhages are principally the tearing of the membranes due to overstretching, and rupture of the blood vessels. To produce a tear means the existence of great cranial stress. Since the latter is frequently the result of protracted, difficult labor, where instrumental delivery is practiced, the obstetrician must bear in mind that the force used in forceps application is not to be excessive or not to be applied to the wrong diameter of the head, as for example the antero-posterior. In the latter case the vertical elongation of the head is more than anything else apt to cause overstretching and tearing of the meninges. The forceps is a useful instrument which in many instances has been responsible for saving lives, but it may also be responsible for injuries to fetuses leading to consequences which have a great bearing upon the later physical and mental development of the child.

The preventive aspect of the subject under discussion lies in the consideration of all forces that are liable to lead to tearing of the meninges and of the blood vessels. Wrong presentation and position of the fetus, all other causes of difficult labor, prolapse of umbilical cord, the use of instruments or various manipulations in the delivery of the fetus, are all factors, whose rôle cannot be overestimated in the production of cerebral hemorrhages and of tearing of the meninges. Besides the preventive phase let us consider briefly the therapeutic aspect of meningeal hemorrhage. With a certain degree of possible errors supratentorial hemorrhages, generally speaking, present a some-

what different clinical picture from the infratentorial type. In the former the blood spreads over the hemispheres of the cerebrum; in the latter over the hemispheres of the cerebellum but also into the medulla. In the former the blood cannot go beyond the lower surface of the tentorium; in the latter the blood reaches the subarachnoid space and may extend into the spinal canal.

For these reasons in the supratentorial hemorrhage at birth one finds a bulging fontanelle and a group of nervous phenomena, such as sleeplessness and great restlessness, convulsive seizures, and the condition persists. In the infratentorial cases there is considerable depression, apathy, somnolence, early cyanosis, vasomotor and respiratory manifestations, and rigidity of the neck muscles. In view of the anatomic differences, respiratory and other bulbar disturbances will not be observed in the supratentorial cases. Cyanosis is late and, when it does appear, is not pronounced in the supratentorial hemorrhages, but is early and very much pronounced in the infratentorial cases. The anterior fontanelle bulges early in the supratentorial, but slowly in the infratentorial cases.

For the anatomic reasons just mentioned, in infratentorial cases lumbar puncture may be of considerable benefit. Advocated first by Devraigne[4] he was rapidly followed by others, and favorable or very satisfactory results have been reported in the literature. Frequently the withdrawal of spinal fluid needs to be repeated. In some cases, as in that of Lippman,[5] one puncture may suffice. His patient presented convulsions, cyanosis, and rigidity. As the convulsions increased in intensity, Lippman removed 25 c.c. of bloody spinal fluid and complete recovery followed. In Green's[6] case there were convulsions, cyanosis, and apnea. Four punctures were made and 5 c.c. of bloody spinal fluid were removed each time; all the symptoms cleared up. J. M. Brady[7] has recently reported very favorable results from lumbar punctures and removal of some spinal fluid. In the supratentorial cases lumbar puncture cannot be of special avail as the blood cannot reach easily the subarachnoid cavity. Surgical therapy is almost the only resort. Early craniotomy is directly indicated. Favorable results from the very nature of the condition can be expected only when an operation is performed very soon (within a few days) after birth. After the clot has already produced damage to the cortical tissue, no relief can be expected. Cushing (*Surgery of the Head*), who obtained four complete recoveries in nine cases, is of the opinion that no hesitation should exist in operating on such young infants in view of the fact that the newborn can withstand cranial better than any other surgical operation, that much less traumatism is created by an operation than by the passage of the head through the pelvis during birth. Cushing claims that with proper hemostasis and proper preservation of the body temperature during the opera-

tion, the possibility of surgical success is assured.   In his fatal cases he found extensive extravasation over entire hemispheres; the patients were in a dying condition.   Not too much, he counsels, should be attempted at one sitting, and a secondary intervention is advisable.

Henschen[8] advised in the supratentorial cases, aspiration of the cranial subdural space which should be followed by an incision through the coronal suture.   J. M. Brady[7] suggests in the supratentorial cases to perform first a lumbar puncture and immediately afterwards to make an incision below the parietal suture.   It seems logical that in all cases indicating increased intracranial pressure at birth, before a definite localizing diagnosis is made, lumbar puncture should be resorted to at once, since in the infratentorial group it is of definite therapeutic value, and in the supratentorial cases the diagnosis may be promptly established.

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REPORT OF A CASE OF ACQUIRED ATRESIA OF THE VAGINA AND THE OPERATIVE RESULT*

By Hermann Grad, M.D., F.A.C.S., New York

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ACQUIRED atresia of the vagina from caustics, applied as a therapeutic measure, is very rare.   The following case recently came under my observation.

Miss V., aged twenty-seven, consulted her physician about a leucorrheal discharge prior to her sailing for an extensive trip.   Her physician told her that, as there would be no opportunity for a course of treatment he would make one strong application, the effects of which would wear off by the end of her ocean voyage. Her physician made the application and she was immediately seized with great pain and had to go to bed.   She suffered great pain all night and the next morning went aboard the ship on which she was sailing.   During the entire ocean trip she remained in bed and was in constant pain.   On landing she was sent to a hospital in London, where a diagnosis of carcinoma of the cervix was made and a specimen was taken for examination and was reported negative.   Under local treatment and irrigation she improved rapidly and in ten days was able to leave the hospital.   There was no further vaginal discharge and she considered herself recovered.

*Presented at a meeting of the New York Obstetrical Society, October 9, 1923.
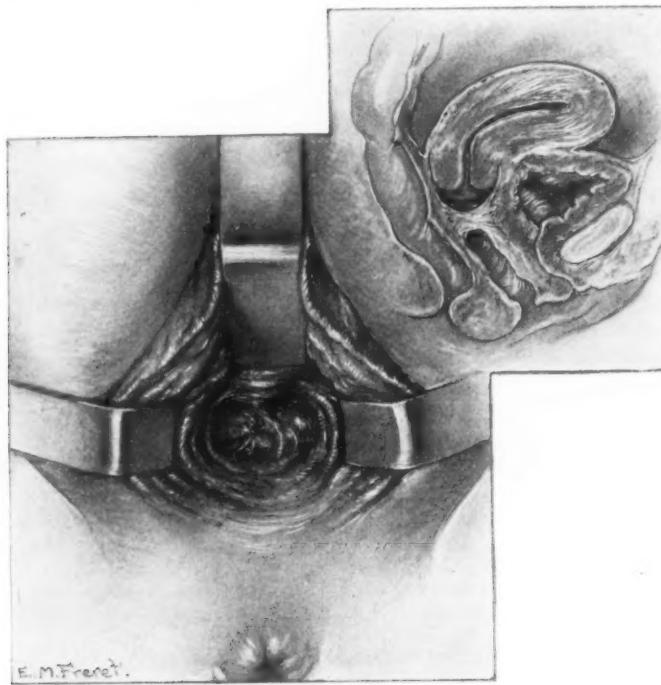
Fig. 1.—Atresia vagina.   Scar tissue in front of cervix uteri.   Right hand figure shows side view.
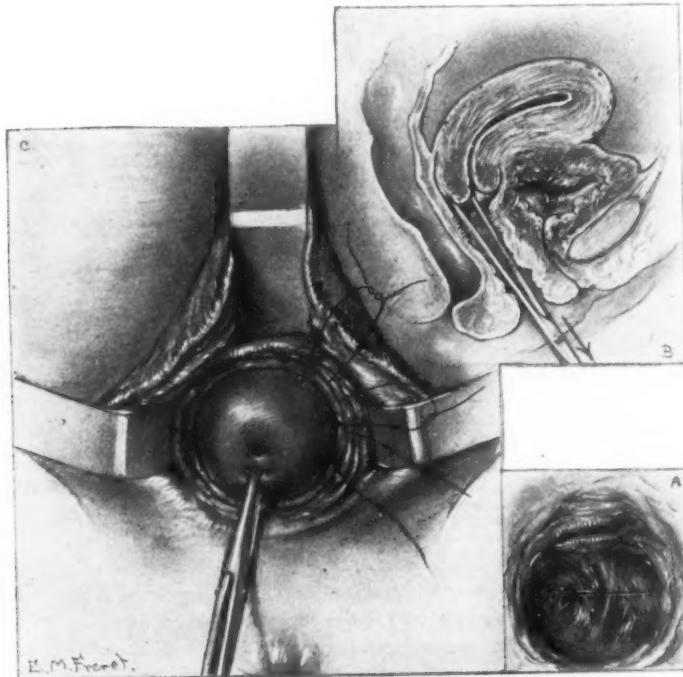

Fig. 2.—A, Shows incision in scar tissue; B, cervix uteri grasped with volsellum; C, cervix encircled by scar tissue.

When her next menstrual period came around she was taken with severe abdominal cramps but no flow occurred. This continued for six months. Previously her menstruation was perfectly normal. During August, 1923, she was obliged to go to bed for five days, with more pain than during the previous five months. She went to Paris and at the American Hospital was told that the only thing for her to do was to submit to a hysterectomy. She then came home and presented herself to me for examination. The latter revealed a short vagina with a complete atresia at the upper third; the cervix could not be palpated; the uterus appeared to be enlarged and the adnexa appeared to be normal. Further inquiry brought to light the fact that the patient had nitric acid applied to the uterus and cervix. The atresia was the result of this application.

The patient was sent to the hospital and under anesthesia the scar in the vault of the vagina was incised. Immediately about four ounces of dark blood escaped, evidently retained menstrual blood. The problem was how to prevent the recurrence of this atresia, and the thought came that if the cervix, after it was dug out of the adhesions, could be pulled down sufficiently so that normal mucous membrane could be sutured around it like a cuff a subsequent atresia will be prevented. Accordingly the incision was enlarged and the cervix dug out of its adherent position and pulled through the incision in the scar of the vagina. The vaginal mucous membrane was then sutured to the cervix. The cervix was red and denuded of its mucous covering. The wound healed and the cervix became covered by an epithelial lining and the patient had one scanty menstruation. The drawings show the steps of the operation.

FORTY EAST FORTY-FIRST ST.

HEMATOCOLPOS IN A CHILD OF SIX WEEKS*

BY G. L. MOENCH, M.D., NEW YORK CITY

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RECENTLY I was called to see a child of six weeks (L. K., Borough of Brooklyn, 1923, No. 2298, Office of the Chief Medical Examiner of the City of New York) found dead in bed at 6 A. M. by her mother who thought she had crushed her as there was bloody froth at the baby's mouth. The mother had given the baby the breast two hours before death but the child had not nursed well. There was no history of cough, fever or any illness. Urine and feces had been normal; the infant had always been weak and had cried only feebly.

The autopsy showed a fairly well nourished, apparently perfectly normal, white female child about six weeks old. External signs of violence were absent. The heart showed a large patent foramen ovale. The lungs were firm, small and pink and not fully expanded. There was marked pulmonary edema. The peritoneum of the anterior wall of the lower abdomen was smeared with old tarry blood. The left ovary was normal for the age of the child; the right one, however, was composed mainly of a cyst about the size of a large pea filled with old blood. The uterus measured fifteen by eight by five millimeters and was set on a round cystic mass the size of a golf ball which proved to be the dilated, but otherwise normal, vagina filled with old blood. The hymen was imperforate; the cervix slightly

eroded. The interior of the uterus was clean; the endometrium that of a child of six weeks. There were no evidences of hemorrhage anywhere else in the body and the rest of the autopsy was negative.

Microscopic sections simply corroborated the gross findings; the right ovary showed the hemorrhagic cyst which had no lining; the rest of the ovary was like that of any infant as was also the left ovary. The tubes were normal and did not contain any blood; the vagina was normal.

Diagnosis.—Congenital atelectasis of the lungs; pulmonary edema; patent foramen ovale; hemorrhagic cyst of right ovary; hematocolpos; erosion of cervix.

It is difficult to arrive at any definite conclusions about this case. I believe there are two possibilities to consider; one is precocious menstruation, the other, an acute inflammation with hemorrhage. While it is true that infants sometimes have a bloody vaginal discharge soon after birth, this is hardly ever more than a slight amount of bloody mucus. A definite hemorrhage, such as was present in this case, does not occur, but of course is within the range of possibility. However, if we accept precocious menstruation as an explanation here we must also assume that, after the hemorrhage occurred, degeneration of the endometrium and restitution to that ordinarily found in the infant took place as no signs of precocious endometrial development were found at the time of death. Nevertheless, the hemorrhagic cyst in the ovary would favor such an interpretation.

The second possibility, that of an acute inflammation, seems less probable. We would have to presuppose an acute vaginitis accompanied by hemorrhage and by extension into the right ovary. The only support for this hypothesis is the fact that a number of pathologists claim that an imperforate hymen is never congenital but always due to an inflammation.

I do not believe that the slight congenital erosion of the cervix, present in the case, can in any way be made responsible for the hemorrhage. A hemorrhagic diathesis likewise seems improbable as no lesions indicative of such a condition were found.

THIRTY EAST FIFTY-EIGHTH STREET.

Society Transactions

THE AMERICAN ASSOCIATION OF OBSTETRICIANS, GYNECOLOGISTS AND ABDOMINAL SURGEONS

THIRTY-SIXTH ANNUAL MEETING

PHILADELPHIA, PA., SEPTEMBER 19-21, 1923

(Continued from March issue.)

DISCUSSION

DR. JAMES A. HARRAR, New York City.—This is an operation which every one who performs cesarean section frequently should know because it is sometimes of distinct value. Every now and then there will be cases that demand such an operation. The description sounds rather elaborate, but in the performance of it, it is interesting to see how easily one can dissect through the areolar tissue with fingers and come upon smooth purplish surface of the uterus ready for incision. There is very little cutting done after the abdominal wound is open, until the surface of the uterine muscle is reached.

DR. OTTO H. SCHWARZ, St. Louis, Missouri.—The time this operation requires is, I think, of great importance. The cases in which the operation seems applicable have already been subjected to the strain of a prolonged labor, traumatism, and in some instances, an anesthetic, and therefore are notably poor surgical risks.

The remarkable results obtained in a series of sixty-four cases at the Johns Hopkins Clinic reported by Harris, in which hysterectomy was done, resulted in only three deaths, and none was due to peritonitis or bacteremia. I feel that this method of dealing with these cases, offers, by far, the best prognosis for the mother.

DR. JOHN O. POLAK, Brooklyn, New York.—Extraperitoneal cesarean section is of particular interest to me as I happened to have had the opportunity of assisting my predecessor, Prof. Jewett, in one of the cases referred to by Dr. Davis. I had not seen the operation again until I saw Dr. Davis do it. The whole point, it seems to me, rests upon whether the patient is potentially infected or not. There is no cesarean section, flap operation, Doederlein operation, or the rehabilitation of the old Thomas operation, that will save the infected patient. I think Dr. Davis will agree with me in this. There are some cases, I can conceive, where the handling has been such, though we have no definite evidence of infection, but where extraperitoneal delivery offers the safest route. We have, of course, in Brooklyn, been doing a modification of the Doederlein operation, the so-called double flap operation of Beck. In this way we have avoided a possible leakage. Patients who have undergone cesarean section die from two causes, aside from hemorrhage, either from a spreading peritonitis, or a general infection. No operation, save hysterectomy, will prevent a general infection. The flap operations will prevent leakage and general peritonitis.

DR. ABRAHAM J. RONGY, NEW YORK CITY.—I think Dr. Polak is right, when he states that if infection has set in, no matter what operation one does, the patients usually die. I have come to the conclusion that no matter how long a woman has been in labor, as long as she has not been traumatized by instruments, I will take a chance with a classical cesarean section. If the woman has been in labor for forty-eight hours or longer, and she is brought into the hospital slightly traumatized from instrumentation, with a torn cervix or vagina, and the baby is alive, pubiotomy is the operation of choice in those cases. I reported before this Association twenty-seven cases of pubiotomy, of which I personally did sixteen, and saved all the mothers, with a mortality to the children of 27 per cent. When the disproportion is out of proportion, pubiotomy must be eliminated; I feel that in such cases craniotomy is indicated, because these patients have a better chance by craniotomy than by any kind of cesarean section you may perform.

We must take into consideration the secondary results of such operations, although personally I have had no experience with the particular operation described by Dr. Davis. If a patient once gets a hernia along Poupart's ligament, there is no way of repairing it and that woman will have a hernia the rest of her life. What happens, if the woman should become pregnant again and has a hernia in the lower portion of the abdomen, which cannot be supported or corrected? The older one becomes, and the more one sees of neglected cases of labor that call for operation, the more one realizes that any operation, which will keep the woman in the operating room the shortest length of time, should be the operation of choice. Occasionally we may sacrifice a badly damaged baby for the sake of the mother.

DR. HUGO O. PANTZER, INDIANAPOLIS, INDIANA.—We all have been impressed with the unfavorable results following cesarean section in infected cases. Sodium salicylate, as an antiseptic remedy, has powerful effect not yet sufficiently recognized by the profession. I had the virtues of this remedy most vividly impressed upon me while in attendance on the von Jacksch's clinic at Vienna, in 1885. A postparturient woman was presented who had developed grave sepsis and, latterly pyothorax, in the obstetric division of the All gemeine Krankenhaus. She had been taken first to the surgical division, but there was referred to the internists' division because the surgeons said they did not operate on dying women. The patient showed a temperature of 104°, fleeting pulse of 180, comatose condition with wild carphologia, very dry skin and tongue, the latter, it seemed, in danger of breaking, as it wagged against the teeth in a muttering delirium. The case seemed absolutely hopeless. Much to my surprise von Jacksch said, "We will give this patient fifteen grains of sodium salicylate hourly, until eight doses are given, thereafter one-half that dose every four hours," and, concluding, "when you return tomorrow our patient will have a moist skin, clear sensorium, and will be asking for food and drink."

Wood, our authority in Materia Medica in those days, taught that sodium salicylate should be given in very small doses, it being a very dangerous remedy. I looked for nothing good to come to our patient. However, to my surprise, von Jacksch's prophesy came true. Since then I have given this remedy extensively, with ever increasing confidence. In quite a number of cases like these under consideration by the essayist I have done cesarean section after large doses of sodium salicylate had been given, preferably by rectum, and have had most remarkable recoveries.

DR. JAMES F. BALDWIN, COLUMBUS, OHIO.—I would like to say a word in regard to the original Porro operation in these cases. I performed the first Porro operation in Ohio, the third successful one in the United States. The operation

was done a good many years ago at two o'clock one morning in a cellar. The woman had an infantile pelvis. The child was alive, the patient's general condition was not bad, but the surroundings were very bad. I carried out a typical Porro operation, brought the uterus out, transfixed it at the cervix, put a rubber tube around, cut the uterus off, and closed the incision around the stump. She made a beautiful recovery, and died only a few years ago. The baby lived several months, dying of some acute throat trouble. I have had a number of cases that were septic, have operated on them, removed a living child, and made a hysterectomy, panhysterectomy if the cervix was bad, and supravaginal hysterectomy (subtotal) under other circumstances. These women have all recovered, with the babies alive.

I noted with a great deal of interest the laparoelytrotomy operation when brought out by Dr. Thomas, but it did not impress the profession favorably and soon lapsed into innocuous desuetude. I would rather do a panhysterectomy or supravaginal hysterectomy, or even a Porro operation, than do the operation the essayist has described.

DR. DAVIS (closing).—I have employed this technic in a class of cesarean cases in which we have very good reason to believe that the classical operation would have proved fatal. Dr. Polak states truly that in cases generally infected with vigorous strains of virulent bacteria, the patient is not rescued by extraperitoneal or intraperitoneal section nor by the Porro operation. From experience I am convinced that, had these twenty-eight cases reported, been delivered by classical cesarean section, nearly all of them would have died within the first few days. The technic is difficult and intricate. There may be a simpler way to arrive at equally good results in presumably infected cases. I believe that it is a method that is worth while. Twenty-six of the twenty-eight cases recovered. At least six of these women have since borne children, two died. One was undoubtedly of the type referred to by Dr. Polak. The other died from pneumonia plus a long difficult labor and a severe operation.

DR. JOHN O. POLAK, Brooklyn N, Y., read a paper entitled **Is Cesarean Section Justifiable in Ablatio Placentae?** (For original article see page 384.)

DISCUSSION

DR. ABRAHAM J. RONGY, NEW YORK CITY.—I have not had as much experience as Dr. Polak in dealing with cases of ablatio placentae, but I have had some rather tragic experiences. There is no question that these tragic cases require the immediate opening of the abdomen, for the reason that very many of them are mistaken for spontaneous rupture of the uterus.

I have had two cases in the last two years. One was a woman in labor forty-eight hours without progress. The family physician telephoned for me to come and see the patient, saying that she required cesarean section. When I saw the patient she was in shock, and I thought the uterus ruptured. I opened the abdomen and found spontaneous rupture of the uterus with the placenta bleeding.

Only recently I had another patient, in the fifth month of pregnancy. She developed pain in the abdomen and went into shock. For a while I did not know what was the matter with her; I could not make out a tumor. When she did not improve, I opened the abdomen and found spontaneous rupture of the uterus. She died. Not only does a case of ablatio placentæ require cesarean section, but we must consider it as an acute abdominal condition with the possibility of spon-

taneous rupture of the uterus, and if we can act early we will save a number of patients.

DR. OTTO H. SCHWARZ, St. Louis, Missouri.—Dr. Polak cites a case in which there was extreme torsion of the uterus, and that this was the primary factor in this case is quite apparent from the picture. However, I do not believe that is a common cause of ablatio placentae. The underlying condition is a sudden rupture of some vessel of small or large size, and therefore I feel the term utero-placental apoplexy is the term which should be applied to this lesion in preference to the term ablatio placentae.

In a recent study which I have previously mentioned, I have noted in a few cases of toxemia that vessel changes occur analogous to the changes which are seen after delivery, so well described by Goodall. I feel these changes are the underlying condition. It is well known that in hypertension intimal changes take place in other vessels of the body. In the hypertension cases the intima of the uterine vessel showed a marked thickening with the other changes. As the degenerative changes advance, its wall becomes definitely impaired. These vessel changes occur in the spongy decidua, and with the increased pressure a rupture is very apt to take place.

I felt that smaller retroplacental hemorrhages are similarly explained. I have demonstrated vessels in the spongy decidua which appear to have more or less aneurysmal dilatation, and under such conditions, I believe rupture can easily take place. These changes take place as well in the veins but it is a different type of change, and with a rupture of such a vessel or the interference with the maternal blood flow, thrombosis may take place. I believe the finding of thrombosis in the uterine wall does not necessarily mean that it is the primary factor.

DR. LOUIS E. PHANEUF, Boston, Mass.—I would like to mention briefly three tragic cases of premature separation of the placenta which came under my observation within a short period of time.

The first patient was taken with a sudden pain in the abdomen while riding on a street car. She was brought to the hospital bleeding and in extreme shock. The diagnosis was made, the abdomen was opened, and it was found that she had ruptured her uterus in the median line. The rent was enlarged and the child was delivered through it. The patient was transfused immediately, and despite that fact died on the fifth day. The second case was one that gave a history of trauma; she had a partial rupture of the uterus near the median line through which the fetus was extracted. She recovered without transfusion and without anything else being done. A year and a half later I did a low cervical cesarean section in her case and she had an easy convalescence. A third case came to my attention within two months. This woman had a pulse ranging from 140 to 150 with a complete separation of the placenta and a dead fetus. The uterine body was ecchymotic but the lower segment appeared to be normal. I did a low cervical cesarean section fearing that she could not stand a hysterectomy and she recovered without transfusion.

DR. JAMES E. DAVIS, Detroit, Michigan.—I want to further emphasize the points that have been placed before you, but I have found that it is a good idea in eclampsia to get a clear picture of the pathology. In the severe cases mentioned by Dr. Polak there is a hemorrhagic condition of the myometrium, and as Dr. Schwarz has pictured greatly dilated vessels. In many cases there is very marked red blood cell extravasation, so that a cross section of the myometrium looks as if the entire structure were involved in the hemorrhagic process. When that is the case, the picture gives the indications for treatment.

DR. POLAK (closing).—Of the three charts I showed you, one represented the traumatic type. We have a large number of these cases in Brooklyn during the Coney Island season. This type of woman is usually leading one child by the hand, carrying another on her arm, and a third in her abdomen. In her endeavor to get on the car after lifting the oldest child on, the car is started suddenly and she is thrown against the seat in front of her. It is surprising how the number of cases of separation of the placenta increase during the summer in Brooklyn. That is the traumatic type.

The second picture was one of the toxemic type, a placenta with numerous infarcts, while the third · slide represented the opaplastic type, with thrombosis in the uterine wall.

We really do not know what changes these vessels undergo that make them more susceptible to rupture, but we do know there are certain cases preceded by toxemia which show separation of the placenta, and they are undoubtedly of the apoplectic type as mentioned by Dr. Schwarz. There are other cases in which there is extreme torsion of the uterus which seems to be a factor on top of the vessel change.

In regard to treatment, there are some of these cases in which we can do a section. But where there are changes in the uterine muscles and when cutting through the uterus, we find it edematous and thrombotive it should come out. In the tragic case we should have a donor ready for transfusion then eventrate the uterus, clamp down on both broad ligaments, and start transfusion. We can then take as long as we want for the operation, for the patient loses no further blood.

DR. ROSS McPHERSON read a paper entitled **Treatment of Placenta Previa.** (For original article see page 403.)

DISCUSSION

DR. EDWARD SPEIDEL, LOUISVILLE, KY.—The subdivision of these cases into the two classes given by the author of the paper is an excellent one. It is surely more rational than attempts at vaginal examination to determine the extent of encroachment of the placenta on the internal os, thereby starting a new hemorrhage and very likely infecting the patient.

The treatment of the condition should be based on this subdivision also, and preliminary to the treatment we should try to prevent infection by simply cleansing and carefully scrubbing the vagina with soap and water and use irrigation afterward. With such a preliminary cleansing I have never seen infection follow vaginal delivery of placenta previa. The course we follow is according to this subdivision. If the child is nonviable the membranes are ruptured and a considerable quantity of the waters allowed to escape; a No. 2 Voorhees bag is then inserted through the cervix, and when expelled the cervix is sufficiently dilated to bring down a leg and allow the woman to deliver the nonviable fetus. In a case further advanced a No. 3 bag is introduced without rupturing the membranes; the woman will have sufficient labor pains to force the fetal head through when the bag is expelled, if not, then the gloved hand is inserted, a foot brought down, and the child carefully delivered in order that it may live. In a case of central placenta previa, if the patient is not near term, say seven and a half or eight months, vaginal delivery can be effected.

DR. ABRAHAM J. RONGY, NEW YORK CITY.—The cases of placenta previa that present themselves during the period of viability of the child, should be divided into two general groups;—those patients that are in labor, and those that are not. In cases of bleeding in the eighth or ninth month, when the cervix is not dilated

and rigid, we have no means of ascertaining whether the placenta previa is marginal or central. In other words, we are groping in the dark, and in these cases I agree with Dr. McPherson that cesarean section is the only operation of choice and by so doing we save the greatest number of mothers and a great number of babies. In addition, I think, every time we do cesarean section for placenta previa the uterus should be packed for possible hemorrhage, particularly the lower segment. In patients, who are two or three fingers' dilated, we can differentiate whether the case is one of placenta previa centralis or one of placenta previa lateralis, and we can select the method of interference. Patients, whose hemoglobin goes down to 70 or 60, due to bleeding, should not be meddled with, and the sooner such patients are delivered the better for the mother and baby. Once a woman has a hemoglobin of 60 or 65, due primarily to bleeding, a second hemorrhage may kill her, even if she loses only a small quantity of blood.

DR. OTTO H. SCHWARZ, ST. LOUIS, Mo.—I would like to ask Dr. McPherson whether in cases in which he does cesarean section he always transfuses before doing that operation and the use of the bag for the control of hemorrhage?

DR. McPHERSON (closing).—In regard to Dr. Speidel's remarks about the Voorhees bag, I will say that the use of the Voorhees bag is a well recognized method of treating these cases. The only objection to it is the danger of its being suddenly expelled with resultant hemorrhage. Theoretically it is cleaner. I have twice had the Voorhees bag expelled before I was able to do anything. The woman had a good hard pain and bled to death before anything could be done. Packing controls hemorrhage until you take it out; if you have such an accident once it is excusable, but if you have the same accident happen twice, it is not so excusable, and that is the reason I prefer packing to the use of the bag.

In answer to Dr. Schwarz about transfusing before doing cesarean section, I do not think it is necessary to resort to transfusion unless there are indications for it. If the patient needs transfusion, I have things ready so that it can be given immediately. If she comes into the hospital exsanguinated, it is necessary to transfuse her before operation. I have seen cases that bled straight through, the blood coming out at the other end; in other words, it went into the vein and came out of the vagina.

I have not made a practice of packing these cases after operation, and I believe that the suturing of the incision is sufficient irritation to cause contraction of the uterus. Dr. Rongy is theoretically correct, but these patients have not bled to death after they were operated on. I would rather not pack them after opening the uterus.

DR. PAUL TITUS AND VERNON L. ANDREWS, of Pittsburgh, Pa., presented (by invitation) **A Study of Frozen Sections Through the Uteri of Women Dying During Labor.** (For original article see page 396.)

DR. LEWIS F. SMEAD, Toledo, Ohio, read a paper on **Acute Pancreatitis.** (For original article see page 431.)

DISCUSSION

DR. FREDERICK S. WETHERELL, SYRACUSE, N. Y.—I should like to report a case I had recently of acute pancreatitis. From an etiologic standpoint, this case was interesting, in that the patient was just eight days over her crisis from

a rather mild lobar pneumonia. She was seen by her family physician because of abdominal pain, was given morphine, and seen again eight hours after that. I saw the case with him, and the clinical picture and physical findings were those of an acute cholecystitis. The patient was immediately sent to the hospital. There an internist saw her. No urinalysis was made during the attack of pneumonia or up to the time of her admission to the hospital. Further examination with better facilities in the hospital disclosed an abundance of sugar in the urine which led us to think of the possibility of pancreatitis. The abdomen was opened by a transverse incision and extensive white plaques, postperitoneally, were seen. An attempt was made to explore the lesser omental bursa through the epiploic foramen, and great difficulty was experienced in getting in there, and all the tissues were extremely friable. A large drain was inserted into the omental bursa and the abdomen closed. The patient died in twenty-four hours. At autopsy there was no evidence of any kind of obstruction of the pancreatic ducts, no cholelithiasis, but very extensive fat necrosis throughout the abdomen.

DRS. CHARLES GORDON HEYD, WARD J. MACNEAL and JOHN A. KILLIAN presented a paper entitled **Hepatitis in Its Relation to Inflammatory Disease of the Abdomen**. (For original article see page 413.)

DISCUSSION

DR. GEORGE W. CRILE, CLEVELAND, OHIO.—I would like to ask a few questions. First, whether during the time these observations were made the temperature ranged high or low. Second, whether the pathologist noted any relation to the changes that take place in the intracellular structures of the blood vessels, the connective tissue, etc. Third, whether he noticed a change in the stainability of the cells of the liver themselves, and whether the acid alkali balance changed.

I saw many pale areas in the liver which might possibly be thus interpreted.

DR. JAMES E. DAVIS, DETROIT, MICH.—I want to ask one or two questions. First, whether lysis of cells in the liver tissue has been controlled; or, in other words, how long after removal of the tissue was complete preservation established?

It is a common observation in general septic conditions within the abdomen to see not only changes similar to the ones we have had pictured in the liver but in the spleen, in the kidney, and in a lesser degree in other tissues. I should like to ask if any observations have been made as to whether the conditions were primarily in the liver or did they show first in other tissues?

DR. W. WAYNE BABCOCK, PHILADELPHIA, PA.—I should like to ask a question with regard to the calcium content of the blood, which usually does not show a reduction corresponding with the reduced coagulation point. Nevertheless, the intravenous use of calcium chloride has been advocated in hepatic and pancreatic disease with a tendency to hemorrhage, and Dr. William J. Mayo had called our attention to the fact that following the use of this drug, operations for these conditions have shown a lessening in mortality of 50 per cent. Is this injection of real value?

In a few cases, using 200 to 500 c.c. of a 2 per cent solution of calcium chloride, I have seen marked improvement follow, but was the improvement due to the calcium? In a supposedly hopeless case of hemorrhagic pancreatitis and in a case of sudden collapse after cholecystectomy the patients rapidly revived after the injection. The dilute solution seems safer to use and less prone to cause a severe reaction than the concentrated solution usually employed. It is possible that our patients would have improved from a simple saline injection.

DR. HEYD (closing).—We found out that there was a difference in the staining affinities in liver cells, alkalization showing in the protoplasm. I personally carried the specimens to the laboratory within two or three minutes after completion of the operation. They were in an excellent state of preservation. We have used calcium chloride in gastric hemorrhage and in chronic jaundice. We have used both the 2 per cent and 5 per cent solution and, as a rule, after the 5 per cent as after the 2 per cent obtained the same reaction.

DR. HENRY SCHMITZ, Chicago, Ill., presented a paper entitled **The Clinical Significance of Chemical and Serum Analyses of the Blood of Uterine Cancer Carriers Subjected to Measured Radiation Doses.** (For original article see page 449.)

DISCUSSION

DR. JAMES E. DAVIS, DETROIT, MICH.—Unless we know something of the modus operandi we cannot get the understanding we need for differentiating the best forms of treatment. I think it is exceedingly profitable to have this subject attacked from the standpoint of physiologic chemistry. After all that has been said, the vital thing to be considered is not altogether the question of whether every cancer cell in the field is killed. A change from what we call a normal cell, or relatively normal, to the cancer cell may go on when all the predisposing conditions are present. We do not understand the change of cells from benignancy to malignancy. I am not so sure even after we have the malignant cell killed but what some of the normal cells may have the conditions right to become cancer cells. Another important point, we may think a cancer cell is killed. The histologic appearance, the chemical tests we may apply, will all seem to indicate the cells are dead, yet I have seen more than once a tissue that if it were examined today one would say it was absolutely beyond the possibility of continuing life, yet if you examine it three weeks later you will find a nest of cells beginning to grow. That brings up the problem that many of our diagnoses made at one period of time may, with all the knowledge we have, be absolutely in accordance with the facts, and we render a diagnostic decision that is not going to hold after a lapse of time which will bring about a revivifying of the cells.

DR. SCHMITZ (closing).—Dr. Davis is correct in what he has said about the study of cancer cells. Let us take a cancer located in an area where it becomes again subjected to trauma or function peculiar to that particular region of the body; it will invariably recur after successful radiation treatment. A cancer of the tongue or of the lip may be treated successfully with radiation therapy, but if that growth is not afterwards removed surgically there will be a recurrence. In the uterus the conditions are different. Physiologically the function of the uterus is arrested and if sexual intercourse is prohibited we will not observe recurrences after radiation treatment.

OBSTETRICAL SOCIETY OF PHILADELPHIA

MEETING OF OCTOBER 12, 1923

THE VICE-PRESIDENT, DR. NORMAN L. KNIPE, IN THE CHAIR

DR. ALFRED GORDON (by invitation) read a paper entitled **Meningeal Hemorrhages of the Newborn and Their Remote Consequences.** (For original article see page 462.)

DISCUSSION

DR. GEORGE M. BOYD.—This study shows the importance of having more closely associated with us the neurologist. It is surprising the amount of trauma the baby seems to be able to endure without the evidence of meningeal hemorrhage, immediate grave injury or remote injury. I would like to ask Dr. Gordon in what proportion of cases of mental defects or permanent injuries of brain origin he has seen, could he positively attribute the injury to trauma of labor and how he feels regarding other conditions predisposing to these injuries such as toxemia, lues and inherited taints. Do not these, in many cases, explain the condition rather than the trauma? I believe that we are more apt to have injuries from too hurried labor than too prolonged labor. It is important to watch the patient and keep in mind the fact that labor prolonged may damage as well as labor hurried. As to the breech, Dr. Gordon has told us there exists a greater proportion of brain injuries and meningeal injury following extraction. This is logical. I am also convinced that prematurity predisposes to these injuries. Ehrenfest, in his book ''Intracranial Lesions,'' laid stress upon the fragility of the vessels and the dura.

DR. PHILIP F. WILLIAMS.—I should like to ask Dr. Gordon to recapitulate the effects of the minute hemorrhages; those commonly supposed to result from prolonged labor rather than faulty application and traction of forceps.

DR. DANIEL LONGAKER.—I believe we obstetricians should lose no opportunity to familiarize ourselves with, and promptly recognize these lesions. The splendid book of Ehrenfest is in line with the excellent paper we have heard tonight. There are some fallacies in this subject that could be alluded to, for instance the fallacy of the original breech and the damage done incident to head-last labors. That is one thing, the after-coming head in a version is another thing. We must not forget that pelvic narrowing directly causes the breech to present; that under these circumstances we do not have the head to fit into the pelvis, which after all is the best pelvimeter. There is no doubt that the bad results attributed to head-last labors are due to the causative pelvic anomaly and not to the head last *per se*. Again and again I have taken internes and allowed them to do, not one, but a number of versions, as high as ten, in one instance twelve, without the slightest fault and without the slightest injury.

So much to illustrate the fallacy of conclusions based on the mere fact of after-coming head as existent in versions in contradiction to original breech. I believe that unskillful application of forceps is capable of doing great harm, even their use in skilled hands is not always unattended by damage. Fortunately in many of these cases this damage done is so great that there are no remote results. The babies die promptly. Diagnostically and therapeutically much can be done in the early stage of cerebral injury, such as prompt and repeated spinal puncture. The clotting time of the blood will usually be found delayed; by injection of whole

blood into the lumbar muscles, (20 to 30 c.c.) the clotting time is shortened and the repeated spinal puncture has a wonderful influence in clearing up some of these cases and preventing what otherwise would be disastrous remote results.

DR. NORMAN L. KNIPE.—I desire also to ask whether Dr. Gordon's results of version were in statistics on old version, or as it has been done in the last year or two? There is a great difference. I was taught that when a child was born up to the umbilicus we must deliver for fear that it might smother to death. That is not the modern idea of version. I wonder whether the same number of cranial injuries occurred as the result of modern version.

DR. ALFRED GORDON.—Dr. Boyd's query in regard to the percentage of defects due to difficult labor is rather difficult to answer. What he said is perfectly correct, that in a number of instances this is not the only element that enters —toxicity and infection, hereditary syphilis, congenital syphilis, tuberculosis, all kinds of constitutional diseases and finally heredity should be considered. Heredity is a very important factor. In such cases the individuals have a peculiar fragility. To give an exact statistical account with regard to defects, mental or physical, of the central nervous system, it is exceedingly difficult, for the reasons mentioned. We are dealing here not with mathematical figures, not with mathematical individuals, but with individuals who may present at the same time all sorts of congenital defects. We cannot say in every case that it is due exclusively to that. I may say that in some cases in spite of heredity of tuberculosis and in spite of heredity of syphilis, the children after a difficult labor are still born normal. I mean so far as gross morphology is concerned. We have the right to say that a difficut labor plays a prominent rôle in the production of trauma. As Dr. Longaker said, children frequently die at birth and if they survive, the above mentioned elements will have their effect: the child who had a tear and hemorrhage in the meninges is less apt to develop into a normal child if he is already congenitally or hereditarily a defect. Children may be born of normal parents, and in spite of a difficult labor, may resist the damage for a longer time than the other kind. To give you exact figures in regard to the exclusive effect of difficult labor is impossible. I have searched the literature in preparing this paper through and through, and it was very difficult to find such data either among the obstetricians or neurologists. I had the subject in mind. It would have been very important to know the figures. It would have been more striking and convincing if we could get exact figures as to the exclusive effect of difficult labor. Prematurity, of course, is a very important predisposing element; Little's disease is due to prematurity. I wish to say that prematurity itself, outside of local trouble is very frequently—I would not say always—associated with hereditary syphilis or tuberculosis or some blood dyscrasia. As to what Little observed and attributed exclusively to the fact of premature birth, we may say syphilis is back of it in a number of cases. Nervous syphilis of the brain, cavities in the cortex and in the midbrain, porencephalon, or other malformations, microcephalus or microgyria, are very apt to produce during birth additional damage, particularly meningeal hemorrhage. The very important point was brought out by the President, and by the other speaker who inquired about minute hemorrhages. We find sometimes accidentally at autopsy minute, very small, disseminated, diffuse hemorrhages. We have no statistics in regard to that. We know that very minute hemorrhages of diffuse character may not produce gross damage such as cerebral diplegia, but they have a special effect upon the mentality of the child. Of course if you have a number of minute hemorrhages in the motor area alone you will have motor symptoms. Minute hemorrhages are apt frequently to delay the mental development of the child. It is a very important subject. Now as far as the effect of version is concerned from a technical

standpoint, I hope you will not ask me to take up a subject of that kind. I am not competent enough to talk about modern version and former version, but the statistics have reference to the old version; I have no statistics in regard to new version. The object of presenting this subject was not for the purpose of teaching you anything, but to bring into closer contact the obstetrician and the neurologist. We know now that in medicine there are so many points of contact in various branches of learning; there is no such thing as pure ophthalmology, or pure obstetrics. We must all call upon and assist each other but if we lock ourselves in our sanctuary and say "We have no right to go out of neurology," or "We have no right to go out of obstetrics," we are the losers. The studies of medicine at the present time are so broad that they open our eyes to the multiple points of contact between various branches. A man who, for instance, deals with cerebral lesions, you will readily understand, has to consider a great variety of diagnostic possibilities before he decides on a cerebral lesion. Look at the biologic situation, the question of metabolism, the question of state of the blood, the question of syphilis, the question of the spinal fluid. There is the greatest interdependence and contact between various branches of medicine and it is exceedingly important that their representatives should know each other more closely.

DR. GEORGE M. BOYD.—I would like to ask Dr. Gordon a question in regard to epilepsy. Has he ever had under his care an epileptic where he felt that the etiology of this trouble could have been in any way attributable to difficult labor? I have talked from time to time, with a number of neurologists on epilepsy and none has felt that the trauma of labor necessarily had anything whatever to do with the etiology of this ancient and mysterious disease.

DR. ALFRED GORDON (closing).—The subject of epilepsy is a very vast one. We have to consider two kinds of epilepsy. One is organic and due to direct damage of the motor area of the brain. Suppose a child had a hemorrhage over the motor area; as long as the clot remains there, it will irritate the brain and produce focal epilepsy, what we call Jacksonian epilepsy. There is another kind of epilepsy, the idiopathic; to cover our ignorance it means a disease by itself. In this kind of cases the clinical manifestations are not confined to one side. Dr. Boyd reports the case of a child born of normal labor, that means without a trauma, but having developed epilepsy. In such a case there is something back of the epilepsy. We often find children born without difficulties and a short time later develop convulsions. In such cases we cannot blame the convulsions on the confinement. There is another substantial cause back of it. The latter is probably constitutional. Constitutional disease, hereditary conditions are at work. There are also cases in which we have generalized epileptic convulsions due to protracted labor, then there is no doubt of local damage, the head was violently pressed upon, the motor area of both sides is doubtless covered with small minute hemorrhages not sufficient to produce paralysis, but sufficient to produce epileptic convulsion. Epileptic convulsion is the result of irritation of the motor area. To sum up, if a child develops epileptic convulsions generalized in character there may be back of it a constitutional morbid element sufficient to produce irritation of the brain, or small hemorrhages over both motor areas. There are so many elements entering into this problem. A boy of 13 suddenly develops convulsions. After Wassermann is taken and proper treatment instituted the child gets better. On the other hand, we find cases in which disturbed metabolism is likely to bring on convulsive seizure. Where this is corrected the convulsions disappear. So in spite of all I cannot give Dr. Boyd a direct answer, except what I said with regard to so many elements which should always be considered. In his particular case, of course, provisionally it is impossible to give the Doctor a reply as to what age epilepsy developed.

Dr. Edward A. Schumann read a paper upon **The Economic Aspects of Abortion.**

From 80 to 85 per cent of all cases of induced abortion occur among married women who have had one or more children and were at the time of the abortion living with their husbands. The commonly held view that illegitimately pregnant women are the victims of the abortions is not true in the majority of instances. The reasons for the constantly increasing number of abortions are largely economic ones, the housing situation in cities and so forth, with the tendency to a low moral fiber, so common among the women of today. The remedy for this condition of affairs is difficult to seek. We have at present legal or punitive methods; second, religious proscription of the practice of abortion; third, education along economic or hygienic lines; and fourth, control of conception. None of these remedies has so far proved of any avail, but it is the opinion of the writer that failing other means, control of conception offers probably the greatest prospect for success. This is a difficult problem, one not yet worked out, but it is the absolute duty of the medical profession to boldly face it and attempt to reach some conclusion.

DISCUSSION

DR. RICHARD C. NORRIS.—If we ought to sanction contraception, how large should each individual family be? When shall it be desirable in the individual family to begin contraception? What laws shall be framed that can be enforced? Undoubtedly a great many useless individuals are brought into the world. Some States have passed laws providing for castration of defectives. I agree with Dr. Schumann that abortion is more common among married women than among the single. I think it is just as futile to attempt to interfere with the law of Nature, such as this is, as it is to contravene the law of gravitation. I don't believe it can be done. I do not think any law in the world can justly settle the problem and as each age comes and goes its standards will vary. Under economic stress the family should not be large. When economic stress is less families should and could be large. I think the less we have to do with this subject the better. We cannot decide for future generations. We cannot predetermine what individuals may prevail, but we, as a profession, should abandon the idealism of the advanced contraceptionists and conclude that contraceptive methods are not to be approved at the present time, in any widespread public manner as through the agencies of contraceptive clinics.

DR. JOHN G. CLARK.—In entering upon any discussion relative to the means of reducing to a minimum the criminally induced miscarriages, we encounter many difficulties. Looking backwards into the remotest ages, we find that the means of inducing abortions were known not only among professional classes but also among laymen. Neither legal measures nor the fear of eternal damnation will restrain women from seeking to have a miscarriage produced when they so desire. As Dr. Goodell said, there were two things a woman would go through hell for, first, to have a baby when she was sterile, and secondly, to get rid of a conception when she feared its consequences.

Relative to the use of contraceptive measures, I am in full accord with Dr. Richard Norris' expression. To put knowledge into the hands of laymen which would control birth rate would in my opinion be a very hazardous proceeding, and who is to sit in judgment as controllers? There are innumerable cases coming under our observation in which there is every argument in favor of contraception, for it is a great cruelty to inflict upon some women repeated childbirths, while for others it is homicidal. However, the question constantly comes up, what are contraceptive measures, and how available are they? As I have studied this situation,

I am very sceptical of beneficial results accruing from the propagation of popular knowledge relative to contraceptive measures, for they are all inadequate. In the stratum of life where such measures would be of great value, the criminal, the mentally deficient, and the poverty-stricken classes, they would not be used. Among the more intelligent classes of people, where it is so essential that children should be born, there is apparently sufficient contraceptive knowledge to limit the birth rate. France is practising these measures at her national peril. I cannot help but feel, therefore, that while contraceptive measures may be of idealistic value, in practical use, they will prove harmful.

Sometime ago a representative of this contraceptive movement came to me and endeavored to solicit my interest in the matter. A United States senator, who is a physician, had said that if several representative Philadelphia physicians would sponsor this movement he would be willing to introduce a measure into Congress which would favor such a propaganda. Feeling as I do, I could engender no enthusiasm for it, because I cannot see how it is possible to limit this idealistic doctrine to safe usage. In our slum districts where there is a high degree of fertility, contraceptive measures are not only impracticable, but would not be adopted. For a woman who is pressed upon on all sides by poverty and the most gruelling conditions of life, with a family already too large, further additions are really tragic, and any measure which would limit the birth rate in such instances would, I am sure, be beneficent, but can it be restricted within legitimate bounds? As we all know, it is not long after a malpractitioner enters upon his nefarious career that his reputation rapidly increases through gossip. A woman who has gone through an illegal miscarriage or abortion is not likely to be secretive about the matter when it comes to passing this knowledge on to some sister who is also in trouble. This is particularily true among married women. Just as gossip concerning these criminal matters is passed on from one to another, so instruction relative to contraception would quickly be disseminated not through restricted professional but through irresponsible lay channels. In these days when sex matters are almost topics for dinner conversation, there is not much that the modern boy or girl of seventeen or eighteen years of age does not know. Among the means for inciting curiosity concerning sex matters, moving pictures and salacious books, which escape the censor's eye, are most pernicious. Even if we possessed any assured means of contraception, therefore, which might be addressed to deserving people it would quickly find its way into the hands of those who would desire to avoid the penalties of immoral living. To repeat, therefore, the whole question seems to me to be an exceedingly dangerous one upon which to touch. As to limiting malpractice, there can be to my mind but one means, and that is, through education, laying stress upon its grave physical dangers and the fact that it is a homicidal act. Here again we are immediately met by a well nigh impossible situation, for everyone of us knows that when a woman applies for illegal assistance, moral or religious suasion is seldom a controlling influence, and even the direct forecast regarding physical dangers has no restraining effect. Dr. Schumann has asked the question as to how we are to limit miscarriages? It is an evil which has existed through all time and will continue to exist. It may be held in stricter abeyance by more drastic laws and further minimized by moral training of young people.

DR. EDWARD A. SCHUMANN.—May I remind the members and the Chair that my paper was not in advocacy of contraception? I am asking for a remedy for the increasing number of induced abortions in our hospital wards.

DR. JOHN A. MC GLINN.—I understood from Dr. Schumann's paper that he advocated contraception as one of the cures for the frequency of induced abortion. It seems to me that this is an intensely difficult proposition to settle. There is no

question but what there are more abortions among married women than the unmarried, for the simple reason that there are more married women indulging in sexual intercourse than the unmarried, so I do not think you need be surprised as far as these statistics are concerned. It is rather striking within the past two weeks I have had three patients in my office who in order to avoid children have resorted to induced abortion. One of them had one child five years ago and became pregnant shortly after and had abortion produced and then later the child was killed by an automobile. She has stopped contraceptive measures and endeavored to become pregnant. On examination she has had sealed up tubes. Now she is perfectly willing to undergo an operation to bear a child. The other two women are "crazy" for children. One marriage is going to result in divorce. We should not ask the Legislature for more laws; we have more laws than we need at the present time and will only have another that will not be enforced because you cannot make people good by legislation. It seems to me the solution of this problem is that the individual has to be taught morals and have a conception of the moral law. It is not much good to preach to them. They will take a chance anyhow. About a year ago I presented a report of five cases where a special pessary was introduced in order to prevent conception. All these women were related to each other; one had a hysterectomy done as the result of infection and nearly died; in spite of this her sister had the same thing introduced. She had a pelvic abscess and refused operation. In spite of her experience her cousin had the same thing introduced; she developed infection. In spite of that a personal friend went over and got the same thing, she became pregnant and the pessary slipped up into uterine cavity. You would think in these cases that experience would have taught these women not to adopt such measures.

DR. BROOKE M. ANSPACH.—Undoubtedly in the upper classes of society the birth rate is low. Some years ago in the Babies' Hospital Campaign to raise money for a new building, I was persuaded to join one of the teams. I went to a rich man, solicited a large contribution, and urged the necessity for conserving infant life. He asked me what proportion of the increase in the population of the United States since the Civil War was due to children born of parents native to this country. I went to some trouble to find out and was struck by the small number of children among native born Americans and the much greater number of children among the foreign born. I think that intelligent people should be given to understand that they have a duty to the State to fulfil, that they ought to raise children and that they should only limit their families by the measure of reasonable necessity. Legislation, of course, is out of the question. It would be quite unwise to attract public attention to this subject, nevertheless, I think Dr. Schumann has brought before us a very vital question, and we can profitably discuss it among ourselves. It is for us to give what information we have, to those who are ignorant.

DR. SCHUMANN (in closing).—I confess to some measure of disappointment. I came here with the request for some remedy to prevent the steadily increasing number of criminal abortions. What is the remedy? I have not heard a single constructive word here tonight. What are we going to do about the abortions? They are here. Like manna on parched soil comes Dr. Anspach's statement that really something ought to be done about it and possibly contraception is the remedy. None of us will say, What are we going to do? If the subject is brought up the medical profession invariably says that is a matter unfit for medical discussion and the abortion rate goes up and up in the meantime. I believe the sooner we realize that this is a condition and not a theory and we have got to do something about these abortion cases in married women, the better. I do not offer contraception as the remedy. I offer it as one suggestion.

Department of Reviews and Abstracts

Collective Review

ESSENTIALS IN ROENTGENTHERAPY OF INTEREST TO CLINICIANS; WITH A CONSIDERATION OF ITS APPLICATION IN GYNECOLOGY

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ROENTGENTHERAPY is a composite of the sciences of electricity, physics, mathematics, biology, and biological chemistry. The scientists who labor independently and conjointly in these different fields look to the clinician for guidance and inspiration in the pursuit of their researches. For through the practical application of the theories evolved in the laboratory, the clinician comes into possession of facts which verify or disprove the scientific claims. In order that clinical criticism may be constructive it is necessary that the clinician be versed in the essentials of the sciences bearing upon the remedies he is employing.

The application of x-ray energy as a therapeutic agent is constantly increasing; it has already invaded almost every medical specialty, and no clinician who is abreast of the time can afford to remain indifferent to it. It is my aim to present to the practicing physician the essentials of radiotherapy in a clinically assimilable form, so that he may prescribe or proscribe this remedy in an intelligent and conscientious manner.

I. THE PHYSICAL FACTORS

A. The Source and Character of X-Rays.—X-rays come into being through a transformation of electrical energy from one form into another, under the following physical conditions. When an electric current of high voltage is made to pass a vacuum of about 5 mm. of mercury, the current will flow from the anode or positive pole to the cathode or negative pole. This attempt is accompanied by the appearance of a diffuse red light around the anode, a faint bluish light around the cathode and an intervening dark space. If the vacuum is still further reduced to about 1/100,000 part of the atmospheric pressure, the anode light will recede, the dark space will temporarily increase, and finally the cathode rays will appear.

The cathode rays are invisible to the naked eye, and result from a dissociation of cathode atoms into ions and electrons. The former

are corpuscular elements charged with positive electricity, they remain in the broken up atoms or travel backwards through the cathode, and are known as canal rays; the electrons are supposed to be negatively charged particles of matter, they travel forward with a rapidity corresponding to 100,000 kilometers per second.

When these electrons are hurled forward from the cathode at this tremendous rate of velocity, and are made to impinge upon a solid medium, such as the anticathode in the x-ray tube, a new form of energy is generated through the breaking up of the atoms in the anticathode, which expresses itself in the emission of x-rays.

The x-rays like the cathode rays are invisible to the unaided eye. They travel in a rectilinear direction, at a rate equal to that of light, 300,000 kilometers per second. They are not influenced by magnetic waves, but they can be deflected the same as ordinary light rays, and possess the unique properties of fluorescence and of penetration of solid media.

B. *What Becomes of the X-Rays After Having Entered the Tissues?*—When a bundle of x-rays, sent forth by the anticathode strikes the surface of the body, a part of these rays is absorbed by the tissues, another part passes through, and still another portion is changed into secondary rays.

The secondary rays consist of three main subgroups which may be briefly described as follows: (a) diffusion or scattered rays, which are merely deflected primary rays, dispersed by all substances, in contradistinction to light rays; (b) fluorescent or characteristic rays, which arise in the tissue atoms, and in addition to being deflected the same as scattered rays, also possess a moderate degree of penetrability, which increases with the atomic weight of the irradiated substance; and (c) the corpuscular or B. rays, which arise in all substances irradiated with x-rays, and whose penetrability depends upon the hardness or softness of the primary rays. The secondary rays have no wave characteristics, are formed of "a stream of electrons," and unlike the characteristic rays, their penetrability is not influenced by the nature of the irradiated substance. According to Dessauer[1] "the carriers of the biological effects are the electrons, of which the corpuscular rays are composed."

C. *The Penetrability and Absorption of X-Rays.*—Spectroscopic studies have shown that the beam of rays as it emerges from the anticathode, consists of a heterogeneous mass of rays of different wave lengths. For the sake of practical utility these rays have been subdivided arbitrarily, into two main groups, short and long wave rays. The differentiation depends upon the variation in the rate of rapidity with which the electrons composing the rays travel. The electrons of the short waves travel far more rapidly than the electrons in the long waves. With the change in the character of the rays, there also follows a change in their penetrating powers and absorption coefficient. So that long wave rays are soft, penetrate less deeply and are absorbed in greater amount, than the short waves, which are hard, have a higher degree of penetration, and are less absorbable. The factor of absorption is also modified by the atomic weight of the irradiated substance, media of greater atomic weight absorb more rays than those of lighter weight.

Notwithstanding the value of the above information, the number

of x-ray burns kept on increasing as the employment of x-ray therapy kept on extending. The burns are frightful and even worse than the third degree burns resulting from ordinary fire. Among the victims were not only patients, but also some of the pathfinders in roentgenology. In the attending personnel the injuries from the x-rays differed in character, from blood dyscrasias, to sterility, and to the development of malignant skin tumors. Not until the principles of filtration were enunciated for the first time by Perthes[2] in 1904, have the frightful results that followed in the wake of x-ray therapy begun to diminish in frequency.

D. *The Principles and Advantages of Filtration.*—Filtration is the process by which most of the soft rays are being eliminated from the ray bundle, through the interposition of a metallic plate of either copper, zinc, or aluminium, of different thicknesses, singly or combined, between the x-rays as near as possible to their point of exit, and the irradiated object.

The advantages of this procedure are: (a) the avoidance of the x-ray burns which are due to an excessive absorption by the skin of soft rays, and which are now absorbed and retained in the filters; and (b) the standardization of the therapeutic agent by obtaining a composition of waves of almost equal length, which also means uniform quality.

E. *The Significance of Homogeneous Raying.*—In 1905 Dessauer[3] formulated the principles of homogeneous raying and upon those principles the entire superstructure of modern roentgentherapy was built up. To obtain a clinical conception of the value and importance of homogeneous raying, let us view this problem in the light in which we pursue the study of the action of drugs in general, and note wherein this electro-magnetic remedy differs.

Drugs are generally subdivided into distinct groups, each of which has a definite and specific effect upon a definite organ or tissue, directly or indirectly through the blood. As a concrete example, digitalis is well known to slow the heart's action and to increase its force. Larger or smaller doses will produce corresponding physiologic effects, and the change in dosage will never alter its properties as a cardiac stimulant. Radioactive energy, on the other hand, changes its specificity with the variations in the amount and the quality administered, so that different doses of x-ray affect different tissues. Besides dosage the effect of roentgen ray energy is also greatly modified by other factors, chief among which are the following: (a) distance between the source of the rays and the irradiated object, which diminishes or increases with the square of the distance; (b) the absorption of the rays by the intervening substances and the tissue, between the organs or tissue we wish to irradiate, and the point of entry; (c) the diffusion and the scattering of the primary rays; (d) the size of the point of entry, large or small fields; (e) the biologic state of the tissue; and (f) the degree of cellular and general immunity enjoyed by the organism at the time it is subjected to the treatment.

Leaving out for the moment the above enumerated factors which influence the therapeutic effect of the rays, and bearing in mind only quantity and quality, we are brought to the consideration of the next important principle in roentgen therapy, namely the equal dis-

tribution of the radioactive energy throughout the irradiated fields. For as Jüngling[4] has stated, "The acknowledged necessary minimal dose must be distributed to the entire danger zone, otherwise the irradiation is valueless."

In radiotherapy, therefore, we have two kinds of homogenuity: (a) qualitative homogenuity, which refers to the rays; and (b) quantitative homogenuity, which means an equal distribution of the remedy to all the parts of the diseased focus. To give these academic facts a clinical interpretation, let us assume that we undertook to treat a case of sarcoma of the uterus. It has been established biologically that the sarcoma dose is 75 per cent of the skin erythema dose. If we proceed to irradiate this organ, without taking sufficient pains to see that each cubic centimeter of diseased tissue receives an equal amount of x-ray energy, the effect will fall short of success. The areas receiving less than the lethal sarcoma dose will be stimulated and the tumor cells will proliferate, while those receiving an overdose will show necrosis, not only of the tumor cells alone, but also of the healthy surrounding tissue, and thus further diminish the natural resistance of the organism against the invasion of the neoplasm. Equal distribution of the proper x-ray dose is hence of vital importance, particularly in the treatment of malignant growths.

F. X-Ray Dosage.—The unit of x-ray dosage is a biologic estimation, obtained in the following manner: When a certain amount and quality of x-ray energy is allowed to irradiate a normal skin surface, for a definite period of time, and if the skin surface will show a pinkish red reaction after an interval of eight days, and at the end of four weeks a dark brown discoloration, then it is assumed that a biologic dose has been given. This amount is calculated as 100 per cent, or as the maximum of skin tolerance, and is termed "the skin erythema dose." Smaller doses will fail to call forth the above described skin reaction, and excessive amounts will be followed by blistering, and later on by necrosis of the irradiated area.

Guided by these morphobiologic phenomena, biologists and clinicians have tested out the reaction of various tissues to the effects of x-rays, and have adopted an arbitrary scale of x-ray dosage. An x-ray dose may hence be defined as a fraction, the whole or multiple of the skin erythema dose, depending upon what we seek to accomplish, stimulation, inhibition, or destruction of the irradiated cells.

We cannot dismiss the subject of x-ray dosage without calling attention to the fact that our knowledge of this phase of x-ray therapy is not absolute, for what we have accomplished thus far with photochemistry, ionization, electroscopy and the other electrophysical aids, was to measure the x-ray energy delivered by the electric apparatus, transfer this energy to the tissues, watch its effects upon and in the tissue, and then only draw biologic inferences.

II. THE BIOLOGIC FACTORS

In the preceding section I have dwelt upon those factors in roentgentherapy which have definiteness and stability, and which may be modified at will to suit our purposes. I shall now consider a group of factors which are indefinite and labile, and which can be influenced to a limited extent only, through indirect means. From the above stated premises it must be concluded that as long as one of the fac-

tors in the roentgentherapeutic equation will, by virtue of its nature, always contain some elements of uncertainty, so long will its solution remain incomplete. We may, however, expect that through a more inclusive understanding of the biologic processes which influence and modify the radiosensitiveness of tissue, and through a better mastery of the means for a more equal and more extensive distribution of the radioactive energy through the tissues, we shall approach a state in roentgentherapy, that will border as closely as it is possible in biology, on the lines of the exact physical sciences.

A. *What Takes Place in the Irradiated Tissues?*—As interest centers chiefly upon the problem of cancer therapy I shall limit my consideration to the morphologic changes which ensue in the tumor and in its surrounding tissues as a result of irradiation. Aschoff and Woegten[5] have described these structural changes as follows: "There is at first a swelling of the cell, then hyperchromatosis, followed by a gigantic growth of the nuclei, vacuolization of the protoplasm and partly also of the nuclear substance. Necrosis and degeneration then set in, and the destroyed and dead tumor cells coalesce into an amorphous mass, which lies as a foreign body in the stroma of the original tissue. This foreign mass of cells calls forth an irritation in the surrounding connective tissue through its liberated toxins; the latter proliferates, replaces the necrotic mass and a scar is formed."

Perthes[6] recorded his observations thus: "The destruction of the cancer bearing area is accompanied by an excessive infiltration of round and connective tissue cells, which force their way in between the epithelial cells, break up the regular and well circumscribed cancer plugs into irregular cancer nests, which are now lying in a network of connective tissue. In the stroma there is an abundance of round cells, among which cancer cells are scattered. The tinctorial properties of the epithelial cells are retained by some, while most of the nuclei are poorly stained. The protoplasm appears as a uniform confluent mass, containing many vacuoles. Most of these spaces are filled with round cells whose nuclei stain well."

Further biologic studies have also brought to light the following salient facts: (a) The effect of the radioactive energy in the tissue does not appear immediately, but after an interval of time, termed "the latent period"; (b) radium or roentgen rays possess no exclusive predilection for tumor cells, they affect all tissues, only in varied degrees, depending upon the dose administered and the biologic state of the tissue; (c) the tissue response, particularly in the surrounding healthy structures, is due not alone to the irritative effects of the toxins liberated by the breaking down neoplasm, but also to the stimulating effects of the rays; and (d) that lymphocytosis and leucocytosis are outstanding morphologic phases in the cancer-bearing tissue examined after irradiation. The clinical value of these facts is important. Because of our knowledge of the "period of latency," we no longer delude ourselves by the absence of an immediate skin burn as an indicator of proper dosage, for it is known that the damaging effects of the rays may appear as late as six months or even later after irradiation. The fact that the rays act upon all tissues should make our object in radiotherapy not only the destruction of the cancer cells, but also the stimulation of the surrounding healthy tissues. The increased regional as well as general lymphocytosis ob-

served in tissues under roentgen treatment brings to our minds the phenomena of inflammation with all its pathologic features and physiologic processes.

Teilhaber[7] was the first to view the problem of cancer from an inflammatory point of view, in the sense that it is the cancer which calls forth the inflammation and not *vice versa*. In his latest contribution he restated his teachings of 1909 and 1914 with still greater clarity and conviction. At the periphery of every cancer-bearing area there is present a distinct zone of lymphocytic infiltration, irrespective of whether the tissue has been irradiated or not. Spontaneous cures of cancer have been reported from time to time by trustworthy authorities. Round-celled infiltration and spontaneous cure place the cancerous invasion in the category of a bacterial infection, in which the leucocytes play the all important rôle of defense and cure. The rôle which these immunity builders and carriers play in the therapy of cancer is in no way inferior. In cancer, instead of microorganism, we have the epithelial cells which try to invade and destroy the connective tissue, and thus bring about the death of the organism. Against this invasion the lymphocytes stand guard, and as long as they can muster sufficient numbers, far in excess of the epithelial cells, so long will the latter be confined to their limitations, and the cancer will fail in its attempt. On the other hand, should the natural forces supported by artificial aids not suffice to call out sufficient reserves, then the neoplasm breaks through the lines of defense, and lays waste to every tissue and organ that lies in the way of its advance. "The lymphocyte thus acts not only as a policeman in the cellular domain of the human economy, but also as an apothecary. He stands guard, prepares the remedy, the immune bodies, and carries it to the most needed places. This explains the enlargement of the lymph glands and the spleen in most of the infectious diseases. It is Nature's attempt to increase the body's immunity through an enlargement of the organs whose function it is to elaborate antitoxins, antibodies, etc. As a negative proof, we may cite the fact that the reason for the increased predisposition to cancer and other diseases in advancing years, is the gradual involution of the lymphopoietic organs."

B. The Radio Sensitiveness of Tissues.—The reaction which takes place in the cells of an irradiated tissue has been termed "radio sensitiveness." Based upon numerous and painstaking morphologic observation, clinicians, pathologists and biologists have finally arrived at conclusions which made possible the formulation of the following laws:

1. The Arndt-Schulz law:—(a) small doses of radio energy stimulate the cells to reproduction and growth; (b) larger doses inhibit their function and stop growth; and (c) very large doses cause their death, through a destruction of their nuclei, and dissolution of the protoplasm into an amorphous stainless mass.

2. The Bergonie-Tribondaeu law:—cells whose differentiation as to structure and function has not yet reached definiteness, are far more sensitive to the effect of x-ray than the more mature cells.

These laws form the basic principles upon which rests all the biologic research accomplished up to the present, in its relation to radiotherapy. As clinical guides they serve fairly well in most instances,

but they are not absolutely accurate and dependable. As an illustration I may cite the oft recorded observations by biologists and clinicians, that morphologically identical tissues react differently at different times, to the same x-ray dose. What is at the bottom of these inconsistencies?

Not being in possession of means with which to observe the biologic changes that take place in the tissue cells and their environment during irradiation, investigators had to content themselves with the more attainable facts, the morphologic appearance of the tissue after treatment. But biologic studies do not permit of final conclusion drawn from end-results alone; such deductions ño more represent the actual process of the biologic change than do postmortem findings interpret truly physiologic pathology.

Radiosensitiveness is a biologic state, and as such changes from moment to moment, like life itself, which Sterling[8] defined as "a continuous series of reaction to environment, ending only in death." In determining, therefore, the radiosensitiveness of a tissue, we must take into consideration not only the morphologic change, but also the biologic condition under which this change was brought about. Only then, when we will be in a position to record and reproduce equal biologic states at will, with the same readiness as we are able to reproduce the physical factors in radiotherapy; only then may we hope to reproduce a uniform reaction of similarly constructed tissue, when exposed to the same dose of radiotherapy.

As a striking example of the influence of environment, nutrition and trauma upon the radiosensitiveness of tissue are the experiments of Voltz.[9] He has shown that—(a) plants raised upon solutions containing different amounts of iron will react differently to the effects of radiation, those containing more iron will be more sensitive than those containing a lesser percentage; (b) plants raised in hot houses, or under exposure to intense artificial light, will be more sensitive to rays, than plants growing under normal conditions; (c) plants through whose soil a galvanic current was passed repeatedly, became more susceptible to radio energy than the control specimens. Later on we shall see how these experiments are clinically verified.

C. *The Rôle of the Blood in Radiotherapy.*—Whether the success in deep radiotherapy depends upon the direct destruction of the tumor cells, or upon a transformation of the physical into chemical energy which ultimately destroys the cancer cells, or as Krönig and Friedrich[10] claim, that the x-ray dose for carcinoma weakens the tumor cells, thus giving the surrounding healthy tissue an opportunity to gain the upper hand, the fact remains that before any of these changes can take place within the cell, the radiant energy must first enter into a biochemical union with it and be absorbed.

Before the technic of deep roentgentherapy reached its present state of efficiency, roentgentherapists met with many difficulties, in bringing sufficient amounts of radio energy into the tissue depths, without injuring the overlying skin surface or the intervening vital organs. They have hence resorted to the intravenous administrations of metallic salts, hoping thereby to bring about a greater absorption of the x-ray energy, due to the greater atomic weight of these metals. This experiment did not stand clinical test; it proved in many cases to be dangerous and was abandoned.

Attention was then turned to the blood, as the safest and most reliable medium for the absorption and transportation of radioactive energy. The soundness of this theory was soon proved by many investigators. Opitz[11] showed that "blood taken from irradiated animals and injected into nonirradiated will produce in the latter's blood changes similar to those observed in the former." To prove that this phenomenon was not due to a foreign protein reaction, he injected normal blood from one animal into another of the same species, without evoking any blood alterations. The same investigator also showed that it requires less radiant energy to effect cellular changes in a neoplasm, when a considerable surface area surrounding the tumor is included in the exposure, than when the tumor alone is radiated. Still more striking is the experiment with isolated tumor tissue, which showed, that an amount of radiant energy equivalent to ten times the dose necessary to sensitize human cancer *in vivo*, will not effect it. All of these experiments demonstrate the supreme value of the blood as the absorber and distributor of radiant energy. In the light of this knowledge, enthusiastic therapists, exposed the whole body to irradiation in the treatment of cancer, so as to obtain the maximum of the curative principle; but this method, too, proved to be impractical and detrimental, for in the anxiety to destroy the tumor a large part of normal tissue, the hematopoietic centers, the adrenals and other vital organs, were also injured beyond the limits of safety.

Pickard[12] has recently published a very unique experiment, which he calls "the extracorporeal irradiation of the blood." It consists of the establishment of an autotransfusion, by which the blood from the radial artery flows into the basilic vein, through a large arched glass tube. The tube is the only part exposed to the x-rays. The outstanding features in this experiment are: (a) the utilization of the hemoglobin in the circulating blood, as the medium for the absorption of the roentgen energy, on account of its atomic weight which is twenty-six times higher than that of any other constituent in the animal economy; (b) the sparing of the rest of the body from unnecessary and perhaps harmful exposures; and (c) the possibility of transmitting the x-ray energy not only to the main pathologic focus, but also to the distant metastasis.

The problem of metastasis very often baffles the logic of the pathologist, the acumen of the clinician and the skill of the surgeon. Quensel[13] reported a series of fifty autopsies on cancer patients, in six of which he found cancer cells in the blood taken from the heart chambers. This clarifies to a great extent the apparent freakish pranks played by malignant tumors, with respect to the dissemination of their secondary foci, and brings us nearer to the explanation of our therapeutic failures, after apparently successful local cures. Guided by this information, and numerous other studies made of late, the localistic conception of malignant disease must be greatly modified, and cancer must henceforth be considered as a general disease, requiring remedies whose influence and effect shall extend far beyond the regional limitations of the primary tumor.

The two principal roentgentherapeutic methods in vogue at present are the large field and the small field exposures. The former method has of late gained in favor, and promises to remain the method of choice. The main reasons advanced for the preference of the large

field irradiation may be briefly summarized as follows: (a) a gain in the quantity of x-ray energy through the additional summation of the secondary rays; (b) a more extensive inclusion of the regional metastasis; (c) a diminution of the risks of stimulation of some parts of the tumor, due to insufficient dosage; (d) a minimizing of the danger of deep burns as a result of cross firing; (e) the assurance of a more uniform and homogeneous distribution of the roentgen ray energy. Significant, as each of these advantages are, the sum total of their benefit depends upon this vital fact, that in the large field procedure larger quantities of circulating blood are being irradiated. In addition to the great absorbing qualifications, and distributing properties of the blood, it also plays the great rôle as carrier of the lymphocytes, which constitute the line of defense against the malignant invasion.

The mobilization of the lymphocytes, in the treatment of cancer, is occupying the attention of radiotherapists for some time. Injections of blood into tumor, before irradiation, are advocated and practiced by Bier; others inject protein substances hypodermatically or intravenously; some resort to preliminary diathermic treatment; and still others advocate provocative irradiation of the tumor, or stimulating irradiation of lymphopoietic organs or those glands of internal secretion which raise the body tone. It matters little which method we choose in order to raise the lymphocytic index, as long as the net result will be an increased general and local hyperemia and the more successful we are in bringing about this condition, the better will the therapeutic effect of the x-rays be.

As negative evidence of the value of the blood in the prevention and cure of cancer, we may quote the following observations. Schwarz[14] noted that anemic skin can withstand larger doses of x-ray than normal skin, and far more than an hyperemic or an inflamed surface. This means that an anemic tissue or person is less sensitive to radioactive energy, and requires larger doses to bring about a normal reaction, or if the normal dose is employed, the reaction may be very slight or none at all. Teilhaber's[15] pathologic findings of stenosed and obliterated blood vessels in the immediate vicinity of cancerous organs, even in those normally well supplied with blood, as the penis or the uterus, lend further proof, that anemia favors the development and the propagation of cancer. Other examples of anemia as a predisposing cause of cancer are the ulcus callosum ventriculi, or the recurrence of cancer at the site of resection. The relation of general anemia to cancer is seen in cachectic patients, who respond very poorly to radiotherapy. Blumenthal[16] epitomized the reason for this fact in the statement that "the defensive reactions in these patients no longer come into play." Grudzent[17] quotes Exner, who wrote in 1907, that "radium therapy had very little or no effect upon cachectic patients." It is therefore a grave clinical error to subject cachectic patients to radiotherapy, for in so doing we are only hastening their end.

D. *The Untoward Effects of X-Ray Therapy.*—With very few and rare exceptions, every individual, even when in perfect health, will manifest a symptom complex, of greater or lesser severity, characterized by headache, anorexia, vomiting, diarrhea, and at times also by a rise in temperature after exposure to x-rays. For want of a better term, this temporary, never fatal, but at times severe reaction, was

termed "roentgen sickness." The German term "roentgen kater" is, I believe, more expressive. It usually sets in from three to eight hours after irradiation, and lasts from two to three days, when it begins to subside gradually. Roentgen therapists and fluoroscopists insufficiently protected from the x-ray effects also experience from time to time a feeling of exhaustion, which is out of proportion to the energy spent. Were it not for the fact that this reaction to x-ray exposure calls forth in some patients so marked a disturbance that they refuse to submit to subsequent exposures, or that they prolong the intervals far beyond the biologic limitation, and so thwart our therapeutic endeavors, investigators would not have spent so much energy and labor to solve this problem and find ways and means of eliminating roentgen sickness from our therapeutic procedure, or at least to ameliorate its effects.

In the early part of the x-ray era it was thought by many that the annoying and unpleasant symptoms of x-ray sickness were mainly due to the inhalations of the nitrous gases generated in the treatment rooms. This theory does no longer prevail, for the modern x-ray laboratories are so constructed that the ozone and the potassium nitrate odors are entirely eliminated; and yet roentgen sickness continues to manifest itself, perhaps in a slightly milder form. The next theory which appears very plausible and has found many adherents was the one of toxicosis, resulting from absorption of the necrotic elements of the broken down tumor cells. But this likewise met with much opposition, for clinicians have observed that very short exposures and skin irradiations, such as are employed by dermatologists, in which no necrosis took place, were also followed by x-ray malaise.

Another group of investigators have studied the differences between the reactions following the exposures of different body regions and came to the conclusion that irradiation of the gastrointestinal tract gives the strongest reaction. Von Bauer[18] claimed that the x-rays produce a necrosis of the mucosa of the digestive and absorptive apparatuses and the toxins resulting from this tissue degeneration are responsible for the x-ray intoxications. Many roentgen therapists voiced this opinion, but subsequent investigations showed that cases suffering from x-ray sickness fail to show pathologic changes in the gastrointestinal mucosa. It was noted, moreover, that irradiations from which the stomach and the intestines were excluded were also followed by a systemic reaction.

Halberstaedter and Simon[19] supported the theory of von Bauer, in the sense that irradiations of the gastrointestinal tract give rise to a far more marked reaction than those of any other region of the body, but that this reaction is not due to a destruction of the mucosa, but rather to an irritation of the nerve plexuses supplying these organs. As corroborative evidence they point to the fact that in deep x-ray therapy, where large doses of electrical energy are employed to effect a necrosis of the tumor cells, the nervous tissue becomes strongly irritated but does not show subsequent degeneration. Their investigations led to the following conclusions: (a) even small doses of x-rays, in comparison with those required to produce a degeneration, are capable of calling forth a strong irritation in the living cells and that the degree of irritation is an inverse proportion

to the radiosensitiveness of the cell; (b) the duration and intensity of the reaction runs parallel to the x-ray dose, and the manifestations of the symptoms are hastened with increasing dosage.

Clinically it has been observed that individuals of a very labile nervous system are more sensitive to x-ray irritation than those of a more stable constitution, and Simon[20] has therefore recommended the administration of sedatives to the highly nervous before the treatment, or what is still more ideal and preferable, a preliminary supportive course of treatment of the nervous system. Keinbrock, Bergonie, and Speder, have defined roentgen sickness as "an early expression of the prodromata in the process of cell degeneration." Werner has advanced the cholin hypothesis as a cause of roentgen sickness, but as its presence after irradiation could not be proved experimentally this theory was discarded. Czepa and Hogler[21] as well as Strauss[22] have ascribed roentgen malaise to an excess of cholesterin in the serum, particularly when the liver is included in the irradiated field. In such exposures the Kupfer cells are injured and are prevented from performing their normal function, of storing cholesterin. The source of the cholesterin is in the nervous tissue which is being acted upon by the soluble lipoids.

Out of this mass of hypothetic and theoretic pabulum offered in explanation of the genesis of x-ray sickness, the theory of "nervous irritation," particularly of the vegetative system, appears to be most plausible, and it finds its fullest illucidation in the recent biochemical studies of kalium and calcium metabolism. Strauss[22] has called attention to the fact that during irradiation the body fluids, particularly the serum, change their electrolytic properties, followed by an increased dissociation of the calcium ions. This produces a sympathicotonia, or what is equivalent to a diminished vagotonia. Zondek[23] has taught us that vagus stimulation leads to a change in the subdivision of the electrolytes, in this sense, that in the cell and in the cell membrane there takes place a relative increase of kalium salts; sympathetic stimulation will result in a relative increase of the calcium salts. It is not pertinent to our present consideration to delve into hair splitting refinements, and establish whether the irritation of the vegetative system changes the kalium and calcium equilibrium, or *vice versa*, but we do know at present that proper body functions depend upon a proper balance between the kalium and natrium salts on the one hand, and the calcium salts on the other. Kraus[24] states "kalium and calcium constitute the two poles between which life and cell function oscillate to and fro," and in another study he[25] emphasizes it, by saying that "kalium and calcium mark time in the direction of our vital forces."

Viewing the problem of x-ray sickness from this angle, the nervous irritation theory can be fully accepted, for under such conditions the vegetative nervous system experiences a disturbance of function without undergoing a permanent physical or chemical change. The clinical course of the malady coincides with this theoretical conception. There still remains one more fact requiring explanation, and that is the difference in the degree of roentgen sickness in irradiating different body regions. This explanation may be found in the realm of endocrinology. The dominance of the ductless glands over the autonomic nervous system, through their control of the kalium and calcium metabolism is now a well established fact. It is no wonder

then that with irradiations in which the ovary, the thyroid, the adrenal, the pituitary or any of the other important internal secretory glands, come within the compass of the x-rays, that a more marked reaction should follow such an exposure, than after one in which they are spared or excluded. Hirsch's observation[26] that stimulating doses of the pituitary, ameliorate the roentgen sickness, in subsequent castration exposures, serves as an illuminating example of the soundness of the theory of the relation of the endocrines to roentgen sickness. Encouraged by these experiences Hirsch adopted organotherapy, in the form of a substitution or supportive treatment, whenever he expects one or more of the endocrines to be damaged or seriously affected by the x-rays in the course of the treatment; his clinical results have verified the rationale of his claim, and deserve trial.

(To be continued.)

Selected Abstracts

Newer Diagnostic Methods in Obstetrics and Gynecology

Roubitschek, R.: The Renal Glycosuria of Pregnancy as an Early Symptom of the Gravid State. Klinische Wochenschrift, 1922, i, 220.

Frank and Nothmann as the first showed that the administration of 100 gm. of glucose on the fasting stomach of women in the third month of pregnancy caused a glycosuria without a perceptible increase in the blood sugar values. In the nonpregnant state the blood sugar must reach at least 0.19 to 0.2 per cent in order for sugar to appear in the urine, while in pregnancy glycosuria is obtained with blood sugar values which are normal or only slightly above this point. Thus the estimation of the blood sugar is indispensable in the performance of the test. However, the test possesses several disadvantages, such as the high price of glucose, the nausea and vomiting of early pregnancy, and the necessity for the ingestion at one time of a rather large amount of sweetened liquid. Hence, Frank, Brinnitzer and others have suggested the utilization of the sugar mobilizing power of suprarenin as a test of pregnancy, as it has been found by several observers (including the author) that sugar excretion very rarely follows the hypodermatic administration of 1 c.c. of a 1/000 solution of suprarenin to the nonpregnant, while in pregnancy this procedure causes marked glycosuria. This suprarenin test is superior to the employment of phloridzin, which causes glycosuria in the nonpregnant as well. Ryser in particular has noted this characteristic action of suprarenin in late pregnancy (with blood sugar values slightly increased), while Brinitzer has shown the same to be true for the early months. Hence, there must exist an increased permeability of the kidneys to sugar in pregnancy.

Roubitschek tried, in sixteen cases, a combination of the two methods which he found thoroughly satisfactory. In only one case of pregnancy was glycosuria not produced. The test is performed as follows: 200 c.c. of tea with 10 gm. of glucose are administered on a fasting stomach. Twenty minutes later 0.5 c.c. of a 1/1000 solution of suprarenin is injected hypodermatically. As soon as sugar appears in the urine, usually in about three-quarters of an hour, 10 c.c. of blood are taken from the median vein, and the blood sugar is estimated by the Möckel-Frank method. He found that, with glycosuria produced, the blood sugar averaged

0.15 per cent, showing that the glycosuria is of renal origin. In two cases the blood sugar values were on the borderline, but both were found also after pregnancy to excrete considerable amounts of sugar. Another patient, an epileptic, evidently had a tendency to pathologic hypergiycemia, but a blood sugar of 0.215 per cent cannot account for a urine sugar of 4.4 per cent, without there being an increased permeability of the kidney in addition. The author recommends his modification as a simple and valuable test, useful in establishing the diagnosis in early pregnancy or in doubtful cases.   E. L. KING.

Köster: Phloridzin in the Diagnosis of Pregnancy. Deutsche Medizinische Wochenschrift, 1923, xlix, 182.

Phloridzin, when injected intramuscularly, produces a glycosuria irrespective of the amount of blood sugar present. In testing kidney function, one decigram is injected. Since during pregnancy there is a heightened irritability of the kidneys, Kamnitzer and Joseph obtained a glycosuria in pregnant women by injecting only two milligrams. Of 300 cases, they had only 6 negative results, or 2 per cent. Köster was not able to corroborate their findings.

The Kamnitzer-Joseph method was employed. Immediately before the test the patient voided. Every half, and in some cases every quarter hour, after the injection, the urine was examined with Nylander's reagent. In order to produce diuresis, she was given 200 c.c. of unsweetened tea at the time of the injection and again half an hour later.

In intrauterine pregnancy at all months of gestation, he had 36.3 per cent failures. In 8 cases of undoubted ectopic pregnancy, there were 62.5 per cent failures. In 18 cases of abortion, there was only one failure, while in 14 cases of incomplete abortion, there were 6 failures. Of 20 cases of suspected ectopic pregnancy, three were positive, but in no case was any evidence of pregnancy found at operation. Frequently the results varied from day to day.

From the results obtained, Köster concludes that the phloridzin test of pregnancy is as unreliable as all other tests heretofore introduced.   R. E. WOBUS.

Schilling, E., and Gobel, M.:   The Diagnosis of Pregnancy by the Injection of Phloridzin. Klinische Wochenschrift, 1922, i, 899.

The authors tried the test of pregnancy devised by Frank and Nothmann. They found it reliable in the few cases in which they used it, though Seitz and Jess obtained a positive reaction only in about 50 per cent of their cases. In view of this suspicion of unreliability, together with other objections to the test, the authors have discarded it. They have not tried the suprarenin test, nor Roubitschek's combined method, but have followed Kamnitzer's lead in employing phloridzin, which was used in 100 cases.

An occasional rise in blood sugar was found, but no direct relationship between the blood sugar values and the outcome of the test was established. This was not surprising, as phloridzin increases the permeability of the kidneys to sugar, so that we are not dealing with a simple filtration, but with a true secretory action.

The results were as follows:

(1) In 10 cases of pregnancy, the test was positive;   (2) In 70 nonpregnant cases, convalescents from various diseases, the test was negative. Some were tested before and during the menses, but no change in the result was noted;   (3) In 11 cases with high fever, a positive result, using all three tests for urinary sugar, was obtained in seven. Hence this method is not applicable to febrile patients;   (4) In 3 cases the Nylander reaction was positive, while the Trommer and the Heine tests were negative. It is therefore recommended that, when the first test is positive, it be checked by the employment of the other two.   E. L. KING.

Küstner: The Diagnostic Value of Adrenalin Glycosuria in Pregnancy.
Deutsche Medizinische Wochenschrift, 1922, xlviii, 1340.

Instead of giving the patient 100 gm. of glucose and examining the urine for sugar, Küstner gives 10 gm. dissolved in 200 c.c. of water and follows this in from 15 to 20 minutes with a hypodermic injection of 0.5 mg. of adrenalin. Thirty minutes, and again an hour later, he examines the blood for sugar. If, by this time, sugar does not appear in the urine, the blood is again examined half an hour later.

The sugar usually makes its appearance in the urine in from three-quarters to one and a half hours. The average maximum blood sugar is 0.141 per cent. He examined 125 women, pregnant from 32 days to 7 months, and found a renal diabetes in 97 per cent of the women examined.   R. E. WOBUS.

Rommert: Glycosuria of Pregnancy. Deutsche Medizinische Wochenschrift, 1923, xlix, 912.

It has long been known that the tolerance for sugar is lessened during pregnancy. The author tested a series of cases by the Brinnitzer-Roubitscheks method, giving 10 grams of dextrose and 0.5 milligram of adrenalin. The adrenalin seemed to cause palpitation and restlessness in some cases. Results obtained by giving 100 grams of dextrose in 400 c.c. of tea without adrenalin also seemed of value. As the glycosuria lessens in three days after the placenta becomes detached it seems probable that this is a typical disturbance due to pregnancy. Küstner, on the ground of animal experiments, felt that the function of the ovary was concerned in the reaction; other authorities, the hypophyseal secretion. The best that can be said is that the glycosuria of pregnancy is a disturbance of the internal secretory gland system.

The author believes that glycosuria can be caused by this method; without substantial raising of the blood sugar (not over 0.21) but with such individual fluctuations to consider that often it does not follow whether the test is strong or weak. He cannot place much dependence on it as a test of pregnancy.
                                                       F. A. PEMBERTON.

Küstner, H.: Renal Diabetes During Pregnancy and Its Dependence Upon the Glands of Internal Secretion. Monatschrift für Geburtshilfe und Gynäkologie, 1923, lxii, 119.

The author studied 125 pregnant women to determine the presence of renal diabetes in them. He found that in the early months of pregnancy, renal diabetes was always present. When a pregnancy was terminated during the first few months, the excretion of sugar did not cease until 72 hours later. As a control, nonpregnant women were studied and the author found that 20 out of 22 nonpregnant women showed, in the presence of a physiologic hyperglycemia, an excretion of sugar in the urine a few days before the menses began. On this last finding the author bases the conclusion that renal diabetes in pregnancy is not the result of the products of pregnancy but is due to a change in the function of the glands of internal secretion. Since this diabetes is present both during pregnancy and during the premenstrual period, it is due to a change in function of the ovaries. This the author claims to have proved experimentally in animals.

After removal of the pregnant uterus, the renal diabetes does not cease until after four to five days. When the ovaries are extirpated, the glycosuria disappears the day after the operation. The ovaries most likely affect the kidneys indirectly through stimulation or inhibition of other glands of internal secretion. Implantation of ovaries from pregnant to nonpregnant animals produced a renal diabetes

after two to four days. This proved that an increased activity of the ovary was responsible for the renal diabetes.

Injections of ovarian extract and corpus luteum extracts were made and it was found that only the latter produced a real renal diabetes. Hence it appears that the corpus luteum plays the dominant rôle.   J. P. Greenhill.

Long and Hirst: Ingestion Glycosuria, an Aid to Early Diagnosis of Pregnancy. New York Medical Journal, 1923, cxvii, 543.

This series of 55 observations brings added evidence to strengthen the assumption that an ingestion glycosuria can be induced in the early months of pregnancy; that it is a valuable diagnostic acid, and that the glycosuria disappears when the fetal and maternal parts are no longer in physiologic relationship. The literature shows a 95 per cent accuracy with the glucose ingestion diagnostic technic in the first three months of pregnancy.

The use of table sugar instead of glucose, and qualitative instead of quantitative tests for sugar in the urine, do not affect the results but make the test more practicable. It is necessary to determine blood sugar only in positive cases to eliminate values over 200 mg. to 100 c.c. of blood. Lactation seems to have no effect on the appearance of glucose in the urine during the test.

The phloridzin technic has yielded no satisfactory results.

Margaret Schulze.

Vignes: The Sedimentation of Red Blood Cells in Pregnant Women. Le Progrès Médical, January 27, 1923, p. 37.

Fahraeus has been able to demonstrate both in vivo and in vitro that the red blood cells possess the property of more rapid sedimentation in pregnant women than in the nonpregnant state. He proves this by isolation of a small segment of vein which is tied at both ends. If then the vein be held in a horizontal position for fifteen minutes and a hypodermic needle introduced at the upper extremity of the portion of vein isolated, one will be able to draw off only clear serum. The foregoing holds true only for a gravida and not for a nonpregnant woman.

Further study, by Vignes, has shown that the rapidity of sedimentation varies directly with the duration of the pregnancy. He also found that this same property was present in such pathologic states as tumor formations, acute infections, etc.

That this increased rapidity of sedimentation was due to a property of the blood plasma and not of the red blood cells was shown by experiments in vitro where washed cells showed the normal rate of sedimentation in physiologic saline, while seemingly normal cells showed an increased rate when introduced into the plasma obtained from a pregnant woman. Vignes attributes this to either a diminished viscosity of the plasma or to a changed surface tension, or most probably, to the diminished specific gravity of the plasma, finding that the rate of sedimentation varies inversely with the specific gravity of the plasma.

Theodore W. Adams.

Molnar: Diagnostic Value of Sedimentation Time of the Red Corpuscles in Gynecology. Zentralblatt für Gynäkologie, 1923, xlvii, 845.

The writer confirms Linzenmeier's postulates that (1) a sedimentation time, less than thirty minutes, is evidence of acute inflammatory process except in severe intraabdominal bleeding; and (2) that less than an hour may indicate the presence of virulent organisms, while over two hours suggests the absence of even latent infection.

He believes the test to have value (1) in the differentiation of inflammatory and noninflammatory tumors of the adnexa; (2) in fixing the time of operation in inflammatory conditions and altered positions of the uterus with complications; (3) as an indication of possible adnexal disease when curettage is indicated; (4) in differentiating between salpingitis and extrauterine pregnancy taking into consideration the symptoms; and (5) in general, in gynecologic conditions of inflammatory origin.   LITTLE.

Stein and Arens: Roentgenograms of the Fetal Skeleton as a Positive Sign of Pregnancy. Journal American Medical Association, 1923, lxxxi, 4.

Stein and Arens make use of roentgenograms to confirm the existence of a pregnancy, to diagnose presentation, and to differentiate pregnancy from other abdominal enlargements. Four hundred cases were used for their examinations and in only three cases were they able to diagnose pregnancy before quickening. They speak very highly of the method as a diagnostic means in the last trimester.
                                                                                    W. KERWIN.

Roberts: Oxygen Inflation of the Peritoneal Cavity for Radiographic Purposes. British Medical Journal, 1920, No. 3124, p. 742.

The method of the author is to prepare the patient with the use of castor oil and restriction of solid food. The oxygen is injected with a fine needle introduced about one inch below and to the left of the umbilicus. In an ordinary adult, not over three or four liters are introduced. After the examination is completed, the needle is reintroduced and the gas allowed to escape. If the gas is not removed, absorption takes five or six days as a rule. He thinks the dangers are largely theoretical, having had no evil consequences in fifty cases. Most of the discomfort is obviated by the removal of the gas at the end of the examination. Various postures are used for different sorts of examinations. He states that the female pelvic organs are visible but that it is difficult to distinguish a solid ovarian tumor from a uterine fibroid.   F. L. ADAIR.

Coliez, Robert: The Artificial Pneumoperitoneum in Gynecology. Gynécologie et Obstétrique, 1921, iv, 562.

The author gives a brief review of the literature. He mentions four positions which have been advised in this method of examination: (1) knee chest position with the tube under the table, the rays directed vertically; (2) vertical Trendelenburg position with the rays directed perpendicularly toward the table; (3) lateral Trendelenburg position with the rays directed horizontally, either dorsal-ventral, or ventral-dorsal; (4) simple dorsal Trendelenburg position with the rays directed laterally. The author considers this method of great value, without any special danger if properly carried out.   F. L. ADAIR.

Peterson-Cron: Transuterine Gas Inflation. Journal American Medical Association, 1923, lxxxi, 980.

The Rubin technic with slight modifications was used to determine the patency of the fallopian tubes and with the aid of pneumoperitoneum roentgenographs made for the purpose of diagnosis. They used carbon dioxide under a maximum pressure of 200 mm. of mercury, but expressed the belief that a higher pressure can be used with safety. In 36 cases of sterility, 13 conceived after the use of gas inflation, and 10 resulted in full term pregnancies, while 3 had spontaneous abortions. They divide the question of sterility into groups, the younger group of women offering

a greater chance of conceiving. They observed during operation rupture of the infundibulum about one inch from the fimbriated end under a gas pressure of from 250 to 350 mm. of mercury. The criteria on which the patency of the tubes is based are four: (1) a manometer reading below 200 mm. of mercury; (2) the sound of the gas passing through the tubes, detected by auscultation over the symphsis; (3) pain in the upper abdomen when the patient is in the sitting posture; and (4) roentgenography or fluoroscopy. About 50 per cent of the women who complain of menstrual cramps are relieved after the inflation. It is now the method of treatment for dysmenorrhea at their clinic and in several hundred cases of transuterine gas inflation, there have been no ill effects. In two cases of early pregnancy, undiagnosed, gas was passed without causing abortion or any injury to the fetus.

WM. KERWIN.

Impey: Pneumoperitoneum of the Pelvis as an Aid to Gynecologic Diagnosis. Edinburg Medical Journal, 1922, xxviii, 21.

The author from personal observation reports in detail the work being done at Ann Arbor by Peterson and VanZwaluwenburg on pneumoperitoneum as a diagnostic aid in gynecology. Through this method the organs of gynecologic interest are outlined by the contiguous gas and all extraneous structures, with the patient in the knee chest position, gravitate out of the pelvis. With the injection of gas controlled as to quantity, temperature and pressure, there seems to be very little danger in this procedure. Carbon dioxide, since it is rapidly absorbed, is preferable to oxygen in this work.

In the presence of contraindications, such as pregnancy or cervical and uterine discharge (purulent or bloody), the gas instead of being introduced through the cannula in the uterus, is run through the abdominal wall. When tubal obstruction is apparent from the manometer readings, the lower route is abandoned. Approximately one thousand cubic centimeters of the gas are required in each case.

With the patient in the knee chest position two cross sections of the uterus are obtained, one at the fundus and the other at the isthmus. The fundus is separated from the bladder by the uterovesical space which under these conditions contains gas. A relaxed perineum alters the position of the uterus and interferes with the view. The broad ligament hanging vertically presents a thin edge so that thickening or tubal involvment is easily noted. The rectum throws a cylindrical shadow along the hollow of the sacrum. Tubal disease, ovarian cysts and fibroids cast shadows that are characteristic. Without the history given, pregnancy has been repeatedly diagnosed at the sixth week.

When bimanual examination is unsatisfactory, the information gained by this method is frequently of value in deciding the necessity of operation. The technic is simple and inexpensive. The method will eventually become a valuable diagnostic adjunct. H. W. SHUTTER.

Deucher W. G.: Digital Examination of the Uterine Cavity. Schweizerische Medizinische Wochenschrift, 1923, liii, 277.

There are many types of vaginal bleeding, especially in women near the menopause where the usual examinations will not suffice for an accurate diagnosis. The case may be curetted and the scrapings examined microscopically with a negative report returned and yet if the uterus be extirpated repeatedly newgrowth will be found, deep in the wall or in some of the appendages. The writer insists that dilatation of the cervix with Hegar dilators plus the use of laminaria will make it possible to examine the uterine cavity digitally and thus assist materially in making an accurate diagnosis. He reports 120 cases and of these, the laminaria were not

needed in 58 cases; in 55 two laminaria were used, and in four cases three were employed. Fifteen per cent of the cases were incorrectly diagnosed by the usual methods but with the digital examination the following diagnoses were made: malignant newgrowth, 2 cases; submucous fibroids, 7; uterine polyps, 6; pregnancy, incomplete abortion and missed abortion, each 1 case. Digital examination of 22 cases of suspected fibroids revealed that 3 were malignant newgrowths, 5 were uterine polyps, and two were really fibroids. Following this type of examination a moderate rise of temperature was observed in ten per cent of the cases only, and rarely was it necessary to use opium to allay pain.   A. C. WILLIAMSON.

Hesse, W.: The Diagnostic Value of Digital Exploration of the Uterine Cavity in Cases of Anomalous Bleeding. Münchener Medizinische Wochenschrif, 1923, lxx, 51.

In this series of 400 patients the dilatation technic of Walthard was used. The cervix is dilated by use of the Hegar dilator plus the laminaria, one, two or three being used as it is considered advisable. In cases where the tents alone were used there was a febrile reaction in but 7 per cent of the cases, while in those where the metal dilators were used the incidence mounted to 42 per cent. As soon as fever is noted the laminaria are removed until temperature has returned again to normal. Uteri which are apparently empty are curetted carefully for microscopic examination. Changes in the mucous membrane and the uterine walls are easily detected and if anything escapes the finger careful curettage afterward will usually prevent a slip. Digital exploration is employed not only in cases of anomalous bleeding with a changed uterus, but also in cases where the uterus and its appendages seem to be normal.   A. C. WILLIAMSON.

Driessen: Diagnostic Curettage. Nederlandsch Maandschrift voor Geneeskunde, 1923, xi, 677.

Driessen calls attention to the fact that, while a minor operative procedure, curettage is not without danger and should therefore not be undertaken under unfavorable surroundings. He feels that when doing a curettage one should always be prepared to do an hysterectomy. To the usual dangers of curettage, namely perforation, septic infection, exacerbation of an existing inflammatory process and obliteration of the uterine cavity, he adds hemorrhage. He cites a case of his own and one of a colleague in which mere dilatation caused bleeding of such severity that a prompt hysterectomy had to be performed in order to save the patient's life. In both cases the bleeding was caused by a malignant chorionepithelioma. Since both of these cases had been curetted previously, they accentuate the necessity of examining all curettings. Driessen feels that while menorrhagia is not ordinarily an indication for curettage, metrorrhagia is practically always, even when the diagnosis seems proved clinically. He applies this rule to fibroids which are to be subjected to radiation. He is inclined to curette for all bleeding near the menopause and calls attention to the care required in making a diagnosis, as the premenstrual endometrium has been mistaken for malignant adenoma. He believes that corpus carcinoma is more common than usually supposed. In eighty-five women over forty which he curetted previous to radiation, he encountered carcinoma thirteen times. He employs either ethyl chloride or ether as an anesthetic.
                                                        R. E. WOBUS.